TO STUDY THE ROLE OF THROMBOELASTOGRAPHY (TEG) IN CORRECTION OF COAGULOPATHY IN PATIENTS OF CIRRHOSIS UNDERGOING INVASIVE PROCEDURES

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Submitted By

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Dedicated

to

my Family

&

Teachers

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LIST OF ABBREVIATIONS

AASLD	American Association for the Study of Liver Diseases
ADAMTS	A Disintegrin Mettaloproteinase with Thrombo Spondin Motifs
AGA	American Gastroenterological Association
AICF	Accelerated Intravascular Coagulation and Fibrinolysis
ALF	Acute Liver Failure
APTTK	Activated Partial Thromboplastin Time
CCT	Conventional Coagulation Tests
CI	Confidence Interval
CLD	Chronic Liver Disease
CPC	Child Pugh Class
CVC	Central Venous Catheter
DC	Dialysis Catheter
DIC	Disseminated Intravascular Coagulation
DVT	Deep Vein Thrombosis
Ds	Disease
EVL	Endoscopic Variceal Ligation
ERCP	Endoscopic retrograde cholangiopancreatography
FFP	Fresh Frozen Plasma
GAG	Glycosaminoglycans
GI	Gastrointestinal
HALT-C	Hepatitis C Antiviral Long Term Treatment against Cirrhosis
HCC	Hepatocellular Carcinoma
LT	Liver Transplant
MA	Maximum Amplitude (TEG)
MASLD	Metabolic associated steatotic liver disease (MASLD)
MELD	Model for End stage Liver Disease
OR	Odds Ratio
PAI-1	Plasminogen Activator Inhibitor 1
PAI -2	Plasminogen Activator Inhibitor 2

PCD	Percutaneous Drainage
PCNL	Percutaneous nephrolithotomy
PEI	Percutaneous Ethanol Injection
Plt	Platelet count
PTCA	Percutaneous Transluminal Coronary Angioplasty
PT/INR	Prothrombin Time/ International Normalized Ratio
Pts	Patients
PVT	Portal Vein Thrombosis
RBC	Red Blood Cells
RDP	Random Donor Platelet unit
RFA	Radio Frequency Ablation
SCCM	Society of Critical Care Medicine
SD	Standard Deviation
SDP	Single Donor Platelet unit
SERPINS	Serine Protease Inhibitors
SSC/ISTH	Scientific and Standardization Committee/International Society on Thrombosis and Hemostasis
TACE	Transarterial chemoembolization
TAFI	Thrombin Activatable Fibrinolytic Inhibitor
TACO	Tranfusion Associated Circulatory Overload
TARE	Transarterial radioembolization
TEG	Thromboelastography
TF	Tissue Factor
TIPSS	Transjuglar Intrahepatic Portosystemic Shunt
TPA	Tissue type Plasminogen Activator
TRALI	Transfusion Associated Lung Injury
UPA	Urokinase type Plaminogen Activator
USG	Ultrasonography
VTE	Venous Thrombo Embolism
vWF	Von Willebrand Factor
WBC	White Blood Cells

ABSTRACT

INTRODUCTION: Thromboelastography (TEG) is a rapid global assessment tool of hemostasis using whole blood. The patients with CLD have a rebalanced coagulation state. Unlike CCTs, TEG is based on the principle of viscoelasticity to measure coagulation initiation, clot formation, clot strength, and fibrinolysis. TEG may avoid unnecessary blood products transfusion in patients with cirrhosis and significant coagulopathy undergoing invasive procedures, hence reducing the cost spent on blood/blood product transfusion and the risk of transfusion related complications.

AIM: The aim of present study was to assess the safety of TEG guided transfusion prior to surgical or radiological interventions in patients with cirrhosis with significant coagulopathy (defined as INR>1.5 and platelet count <50 $x10^3$/µl) and whether use of TEG could reduce the requirement of blood products when compared to conventional coagulation tests (CCTs).

MATERIAL AND METHODS

This prospective observational cohort study assessed the safety of TEG guided transfusions in all consecutive patients with cirrhosis who presented to the departments of General Medicine, Gastroenterology ,Cardiology ,Surgery and Intervention Radiology at Dayanand Medical College and Hospital, Ludhiana and required an invasive procedure. Patient and procedure details were documented in a structured questionnaire after a written informed consent.

Cases shall be selected on the basis of criteria set in inclusion and exclusion criteria for the study and TEG shall be performed in selected patients.

RESULTS: A total 97 patients with cirrhosis with deranged coagulation profile who underwent invasive procedure were included in the study. These patients were given blood products (i.e. fresh frozen plasma (FFP) and platelet units) were given as per TEG results. Of these 97 patients, only 43 (44.3 %) required transfusion of a blood product (FFP /platelet or both).On the contrary all patients (100%) would have been transfused if CCTs were used as a guide. In our study using TEG based transfusion only one patient was transfused both FFP and platelet (1.0% v/s 43.3% in CCT group), only FFP in none (0% v/s 52.6% in CCT group) only platelets were transfused in 42 patients (43.3% v/s 4.1% in CCT group).Clinically significant bleeding was seen in only one patient (1.03%).

CONCLUSION TEG guided transfusion was safe and did not result in a increase in clinically significant bleeding. A significant reduction in the requirement of FFPs was seen when TEG was used in place of CCTs.

Keywords: Thromboelastography, cirrhosis, invasive procedures, blood product transfusion.

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INTRODUCTION

Patients with chronic liver disease (CLD) can become acutely unwell and have to undergo various invasive diagnostic or therapeutic procedures. Conventionally, these patients have been thought to have several coagulation abnormalities and these have been assessed by PT/INR and platelet count[1] The latter are clubbed as conventional coagulation tests (CCTs) and were traditionally used to predict the risk of bleeding and guide blood transfusion prior to invasive procedure However, recent studies have proposed that patients with CLD have a rebalanced state of coagulation due to changes in both pro and antithrombotic mechanisms. Thus, these patients are simultaneously prone to both thrombosis and bleeding[2]. These CCTs are in vitro tests, which may fail to capture the entirety of the in vivo coagulation system dysfunction in this population[3,4]. These are routinely performed and used to guide clinical decisions associated with blood product administration in patients with cirrhosis.

Thromboelastography (TEG) provides a potentially more physiologically meaningful assessment of coagulation status of patient than conventional coagulation tests (CCTs)[5,6]. Unlike CCTs, TEG utilizes viscoelastic principles to analyze coagulation initiation, clot formation, clot strength, and fibrinolysis, offering a comprehensive evaluation of hemostatic function. [6,7]

Thromboelastography (TEG) has broad clinical applications due to its comprehensive assessment capabilities. In the setting of cardiac surgery[8]. TEG is invaluable for managing perioperative bleeding. It helps tailor the use of antifibrinolytic agents and blood product administration, thereby improving patient outcomes. Similarly, in trauma care, TEG is used to quickly assess coagulopathy, guiding the rapid and appropriate use of blood products and hemostatic agents.[9] TEG has role in defining blood products requirement in liver transplant patient and also early predict the risk of development of hepatic artery stenosis post operatively.[10] This timely intervention is crucial to improve survival rates and also minimize massive transfusions.

The implementation of TEG in clinical practice not only enhances patient care but also offers significant economic benefits. By reducing the need

for unnecessary blood product transfusions, TEG helps lower healthcare costs and minimizes the risk of transfusion-related complications such as transfusion reactions, alloimmunization, and infections. Moreover, TEG-guided transfusion strategies have been shown to reduce hospital stay lengths and improve overall patient outcomes, further emphasizing its value in both acute and chronic care settings.

Ongoing research continues to explore the full potential of TEG in various clinical scenarios. As technology advances, the integration of TEG with other diagnostic tools and its adaptation to automated systems may enhance its usability and accuracy.

In summary, thromboelastography (TEG) represents a significant advancement in the assessment of hemostasis, offering a detailed, real-time evaluation of the entire coagulation process.

TEG is poised to become an integral part of hemostatic management in diverse medical fields.

AIMS AND OBJECTIVES

To assess the role of TEG in defining blood product requirement prior to invasive procedures in patients with cirrhosis and significant coagulopathy according to conventional coagulation tests.

Primary Outcome Measures:

1. Safety of TEG guided blood product transfusion prior to invasive procedures in patients with cirrhosis
2. To assess the volume of FFP (Fresh Frozen Plasma), and platelets and cryoprecipitate transfused as guided by TEG, and compare the same to that planned with CCT.

Secondary Outcome Measures:

1. Number of patients with clinically significant post procedure bleeding or hemoglobin drop requiring transfusion with target of 8g/dl.[11]
2. Incidence of TRALI (Transfusion associated lung injury) and TACO (Transfusion associated circulatory overload)
3. Transfusion related side effects, defined as any side effect occurring within 6 hours of infusion of any blood product.
4. Procedure related complications other than bleeding.

REVIEW OF LITERATURE

The liver is essential in maintaining hemostasis in our body.[2,12] The current studies on coagulopathy in cirrhotic patients depict that they have a state of rebalanced, that occurs due to altered hepatic synthesis and functional alterations of both pro- and anticoagulant factors.[2,13,14] The resilience of the hemostatic system decreases further in cirrhotic patients in acute clinical conditions like renal failure, systemic infection or hypovolumia. Conventionally, coagulation tests (CCTs), like (PT) prothrombin time,(APTT) activated partial thromboplastin time and platelet count act as an indicator of general liver dysfunction. However, they fail to capture the complete spectrum in vivo coagulation dysfunction, and lack an insight into various factors such as platelet function, endothelial tissue factor (TF) and blood flow dynamics. Therefore theyhave a limited ability to aid in the decision of whether to administer plasma or whole blood.[3,4] Despite this, these CCTs are commonly used to decide regarding transfusion of blood products prior to invasive procedures in clinical settings.

Thromboelastography (TEG) provides a more physiological and precise assessment of the coagulation system of the patient. It is a rapid point-of-care test to assess hypocoagulable, hypercoagulable, and rebalanced coagulation state. Therefore,TEG may be superior to CCT in guiding blood transfusion requirements in those patients with deranged CCT. Additionally, it can indicate the necessity of anticoagulation therapy when appropriate and assist in selecting the most suitable anticoagulant therapy.[15]

HEMOSTASIS IN CIRRHOSIS

In vivo, coagulation occurs not as a “cascade” but involves three overlapping stages: (1) The initiation phase involves the tissue factor (TF)-carrying cells activation in response to the procoagulant stimulus. This leads to the formation of factors Xa, IXa, and thrombin, which, when formed at an adequate level, initiate the coagulation process further. (2) The amplification phase occurs at the platelet surface where the procoagulant stimulus is amplified, causing platelets to attach, activate,

and hoard activated cofactors on their surfaces; and (3) The propagation phase in which the “tenase” and “prothrombinase” complexes gather on the platelet surface and generate the large amounts of thrombin necessary to form a hemostatic fibrin clot.[16]

Fibrin is a blood clot's mechanical and structural component that holds the cells (platelets and RBCs together).[17] Fibrinolysis refers to the proteolytic degradation of the fibrin mesh of the clot. The plasminogen, plasminogen activators and lytic inhibitors regulate the process. The two enzymes involved in the conversion of plasminogen to plasmin are tissue type (tPA) and urokinase type (uPA) plasminogen activator.[18] The plasmin, plasminogen activators, and plasmin inhibitor belong to the serine protease (SERPINS) family. Fibrin lysis inhibtors namely - plasminogen activator inhibitor (PAI)-1 and PAI-2, act on both tPA and uPA while alpha2-antiplasmin controls plasmin.[19] Thrombin activatable fibrinolytic inhibitor (TAFI) impedes lysis by limiting the ability of plasminogen to assemble itself on the fibrin surface.[20]

In cirrhosis, there is dysfunction in the liver's ability to produce components necessary for blood clotting, as well as portal hypertension, which limits all three phases of coagulation.[21] This results in a fragile balance that can be disrupted by other conditions such as renal failure, gastrointestinal bleeding, or sepsis. These disruptions occur due to interactions between coagulation factors, platelets, and various inflammatory mediators released from the endothelium and WBCs (white blood cells). The coagulation status of patients with cirrhosis is not stable but can return to normal after the resolution of critical illness.

Picture 1: Rebalanced Coagulation in Cirrhosis [22,23]

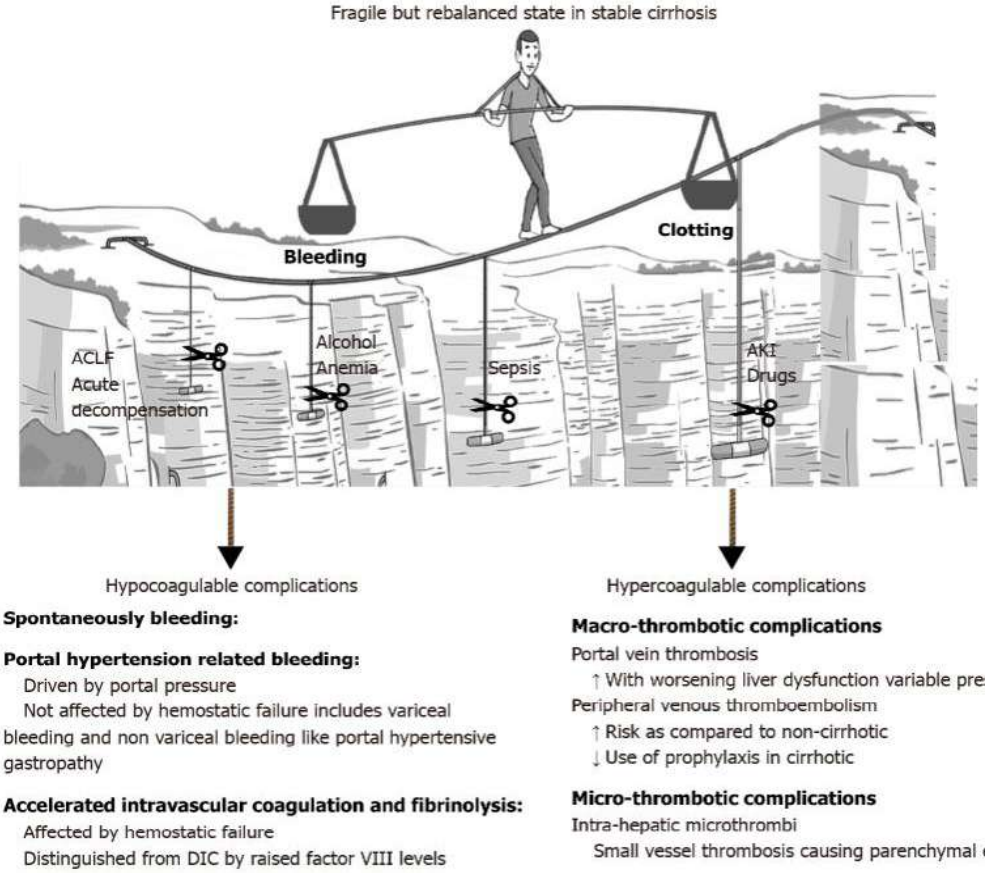


Table A: Alteration of Hemostasis in CLD [24,25]

STAGE	COMPONENTS	HYPOCOAGULABLE STATE	HYPERCOAGULABLE STATE
Primary	Platelets	Thrombocytopenia	Decreased ADAMTS-13 Increased v WF Increased activated platelets
Secondary	Fibrin clot forming clotting factors	Decreased clotting factors II,V,VII,IX,X,XI Decreased fibrinogen Vitamin K deficiency	Elevated factor VIII Decreased Protein C, Protein S, antithrombin and Heparin cofactor II
Fibrinolysis	Clot dissolution	Decreased Factor XIII and Thrombin activated fibrinolysis inhibitor Elevated tissue plasminogen activator Decreased alpha 2 antiplasmin Dysfibrinogenemia	Decreased plasminogen Elevated plasminogen activator inhibitor Dysfibrinogenemia

According to Hoffman's concept of the cell-based coagulation model, bleeding can arise from disorders of primary hemostasis (abnormal platelet plug formation) or secondary hemostasis (reduced thrombin generation and subsequent fibrin clot formation). "The liver has a crucial role in maintaining both primary and secondary hemostasis.[21] The liver is the site of synthesis of most coagulation factors and the anticoagulants of our body, except von Willebrand factor (vWF), factor VIII (only partly synthesized in the liver), and calcium.[26] The decreased synthesis of Protein C and Protein S explains the occurrence of thrombotic events in patients with chronic liver disease despite deranged CCT tests.

Bleeding complications occur commonly in cirrhotic patients and can be due to hemostatic failure or non-hemostatic etiology. “Spontaneous hemostasis-related bleeding refers to an unprovoked hemorrhage of unexplained cause. Spontaneous bleeding is not commonly seen in patients with cirrhosis. Bleeding is typically related to portal hypertension

caused by increased portal pressure rather than hemostatic dysfunction. This was conclusively demonstrated by the failure of recombinant factor VII to achieve control of variceal rebleeding.[27,28] However, such a bleed due to pressure overload can escalate into a hemostatic bleed due to significant blood loss and consumptive coagulopathy. Bleeding (tertiary hemostasis disorder) occurs due to premature platelet or fibrin clot dissolution or excessive fibrinolysis. This is termed as “accelerated intravascular coagulation and fibrinolysis” (AICF) in cirrhotic patients.[29,30]

Hyperfibrinolysis parallels the severity of liver disease: mild systemic fibrinolysis is encountered in 30%-45% of cirrhotic patients, with clinically detectable fibrinolysis in only 5%-10%. AICF has increased level of factor VIII which differentiates it from DIC.[29,30]

Altered fibrinogen i.e. dysfibrinogenemia may result in both hypocoagulable (due to decrease in permeability of the formed clot) and hypercoagulable state which, can manifest as macro- and micro-thrombotic complications. The underlying cause of cirrhosis such as primary biliary cholangitis, metabolic associated fatty liver disease, or primary sclerosing cholangitis can also contribute to the hypercoagulable state.[31]

Thrombotic complications are being increasingly recognized and are being linked to the altered hemostatic balance in such patients. In one case-control study, the patients with cirrhosis were found to have 1.74 times higher relative risk of venous thromboembolism (VTE)(95%CI: 1.54-1.95).[32] A study by **Wu et al.** was suggestive of an increased likelihood of VTE in cirrhosis with an odds ratio (OR) of 1.23 in compensated cirrhotic patients v/s OR of 1.39 in patients with decompensated cirrhosis.[33]

Patients with CLD are at risk of both macrovascular (DVT and Pulmonary embolism) and microvascular complications (intrahepatic microthrombi). The most common macro-thrombotic presentation in liver disease is portal vein thrombosis (PVT), occurring in 8% to 18% of cirrhosis patients. These complications indicate the use of anticoagulant usage in cirrhotics.[34]

The coagulation profile, particularly the prothrombin time (PT) and international normalized ratio (INR) is commonly assessed in cirrhotic patients to gauge the risk of bleeding. However, it's important to note the limitations of using these tests in patients with chronic liver disease.PT and international normalized ratio (INR) measure the activity of a commercially added thromboplastin reagent, was developed to monitor warfarin-treated patients.PT/INR is used as a prognostic marker for mortality in liver disease but has never been validated to predict bleeding risk or guide pre-procedure blood products.[28] PT and APTT indicate the onset of thrombin generation but do not reflect enzymatic coagulation.

Despite their long-standing use as a surrogate for bleeding risk in cirrhosis, the arbitrary cutoffs employed as clinical targets for preventing bleeding lack support from recent association guidelines. Moreover, using fresh frozen plasma (FFP) to correct an elevated INR in cirrhosis does not correct deficiencies in coagulation factors, particularly thrombin (factor II) production, and can exacerbate portal hypertension, thereby potentially increasing the risk of non-hemostatic bleeding.[35-37]

De Pietri et al. conducted a study to explore the role of thromboelastography (TEG) in guiding the use of blood products (FFP and platelet)in cirrhosis patients with severe coagulopathy before an invasive procedure.[38] In this randomized study, 60 patients were assigned to either a TEG-guided group or a control group with similar baseline characteristics. Patients in the TEG group received fresh frozen plasma (FFP) if the r-time exceeded 40 minutes and platelet transfusion if the maximum amplitude (MA) was less than 30 mm. In contrast, the control group received FFP if the INR was above 1.8 and/or platelet transfusion if the platelet count dropped below 50 x 10^9/L. The primary outcome was the utilization of blood products (FFP or platelet units), and secondary outcomes included occurrences of bleeding, transfusion-related side effects, and procedure-related complications. According to the study protocol, all patients in the control group received blood product transfusions, compared to only 5 patients in the TEG group (100% vs. 16.7%; $P < 0.0001$).Additionally, none of the TEG group received FFP alone (compared to 16 in the control; $P < 0.0001$), 2 received platelets

(compared to 10 in the control), and 3 received both FFP and platelets (compared to 4 in the control, which was not statistically significant). Post-procedure bleeding occurred in one patient from the control group following a large-volume paracentesis. The study concluded that INR does not reliably predict the risk of bleeding related to procedures, and the administration of FFP does not necessarily correct INR levels or reduce bleeding events.[39-41]

The most common hematological abnormality in patients with liver disease is thrombocytopenia. In vitro data depicts that a threshold of 50-55 × 10^9/L is necessary for adequate platelet activity, and levels below this range fail to promote thrombin generation.[11] However, the platelet function associated with primary hemostasis (i.e. adhesiveness and aggregation) has not been evaluated. Current guidelines recommend platelet transfusion before high-risk procedures, or in patients with on going bleeding and platelet counts < 50 × 10^9/L. However, this indication lacks a definite evidence that prophylactic platelet transfusion is able to enhance and achieve a balanced hemostasis.[29,35]

In patients with cirrhosis beside platelet count, platelet function is also altered.[42] In patient with hepatorenal syndrome platelet dysfunction occurs due to decreased serotonin in alpha granules and dysregulated metabolism of thromboxane A2. Sepsis and endotoxemia can also alter platelet function.

Recently, fibrinogen levels have replaced INR to couple with platelet count in the evaluation of bleeding risk. Nevertheless, fibrinogen levels do not account for the synthesis of abnormal fibrinogen in cirrhotic patients caused by hypersialylation of the fibrinogen, leading to impaired fibrinogen-to-fibrin conversion.[43]

Different activators can be introduced into blood samples to improve the assessment of various stages in the clotting process. Conventional thromboelastography (TEG) typically uses kaolin, which triggers the intrinsic coagulation pathway. In contrast, rapid TEG utilizes both kaolin and tissue factor (TF), leading to a significant thrombin release and providing initial results (K time) within 6 minutes and alpha angle/MA within 15 minutes.[44,4] This results in rapid TEG delivering findings

approximately 10 minutes earlier than kaolin-based TEG and about 30 minutes earlier than conventional coagulation tests (CCTs) [42] .Such accelerated results could enhance the efficiency of critical resuscitations, enabling real-time monitoring and targeted therapy. However, while activators reduce test turnaround times, they may diminish the sensitivity of viscoelastic tests (VETs), potentially missing subtle changes in coagulation and clot breakdown.

Rotational thromboelastography/Rotational thromboelastometry (RoTEM), utilizes an oscillating pin that rotates +/- 4 degrees 45' every 6 seconds while maintaining the cup's stable position. Additionally, different activator reagents are utilized to investigate specific components of the patient's coagulation pathway.[46]

Thromboelastography (TEG) is an in vitro test that quantitatively evaluates how whole blood forms a clot. This non-invasive test detects and measures the dynamic changes in viscoelastic properties of a blood sample during clot formation under low shear stress. It operates using a specialized system called a thromboelastograph, which consists of two chambers analyzing a blood sample simultaneously to minimize errors in sampling and measurement. Each chamber contains a disposable cup where the blood sample is placed on a platform, with a detection pin suspended in the center of the cup. The cup oscillates around the detection pin within a limited arc of +/- 4 degrees 45' every 5 seconds. Movements induced in the pin are recorded, and changes are measured over time. Initially, the pin experiences minimal movement because liquid blood has low viscosity, and the oscillations of the cup do not affect the pin significantly.[46]

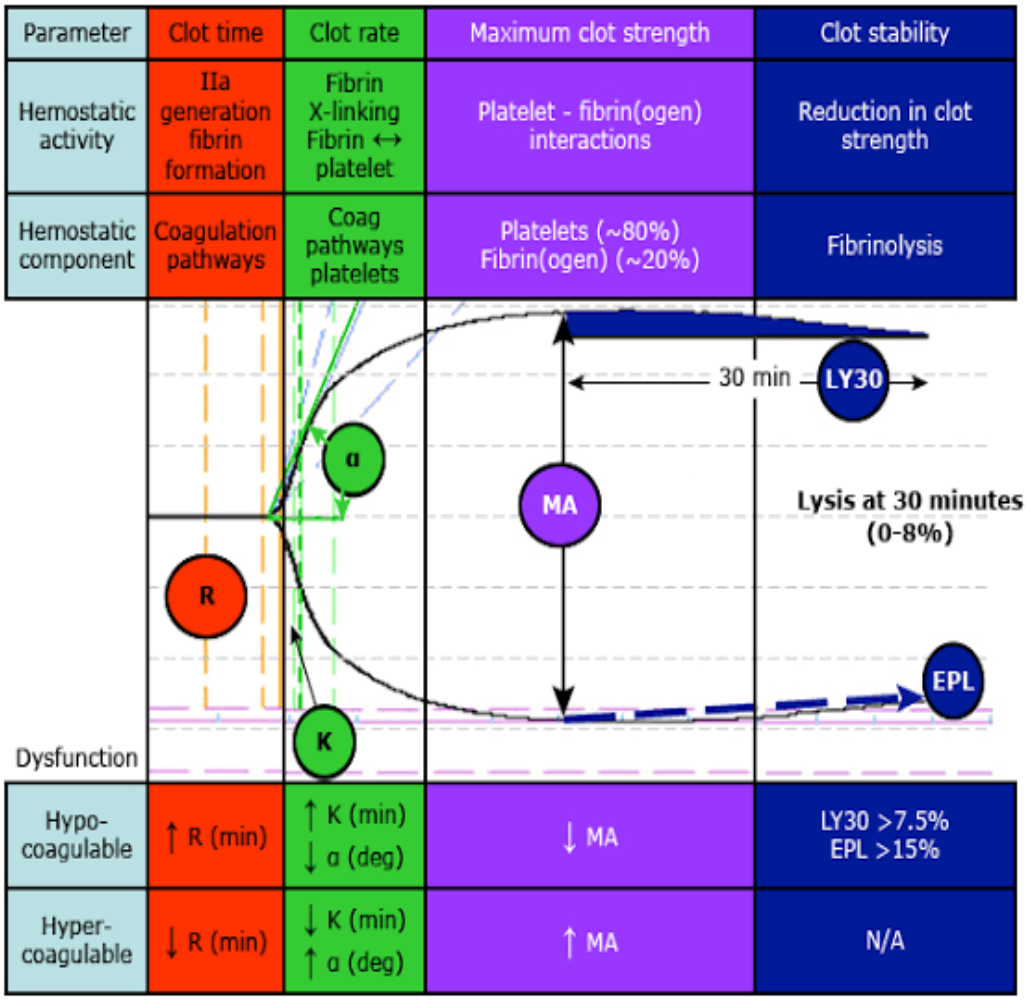
As blood begins to coagulate during thromboelastography (TEG), it adheres progressively to both the cup and the pin, causing the cup's movement to affect the pin. These increasing viscoelastic properties reflect the formation of a three-dimensional fibrin mesh and platelet components within the clot. The greater the clot's viscoelasticity, the more pronounced the pin's movement. As fibrinolysis initiates, the fibrin-platelet structure gradually dissolves, reducing the contact between the clot and the detection pin, thus decreasing induced pin motion. The

thromboelastogram visually represents the amplitude of pin movement recorded over time, with analytical software quantifying these changes. Therefore, TEG assesses the blood's functional capacity to form a hemostatic plug. A newer version employs a resonance technique instead of cup rotation, using vibration to measure the vertical movement of the blood meniscus under LED illumination. This system utilizes pre-measured cartridges, eliminating the need for pipetting and enabling the simultaneous conduct of four blood tests.

Sampling and Procedure[46]

The blood sample is collected through venipuncture into a plastic vial containing 3.2% buffered sodium citrate with a citrate-to-blood ratio of 1:9. The vial is then inverted several times to ensure proper mixing of the blood and citrate. Maintaining this citrate-blood ratio is crucial for accurate test results. Citrate binds to calcium, which is an essential cofactor in coagulation, preventing the blood from clotting before the test begins. A clotted specimen or a vial overfilled with blood will not yield valuable results. The non-clotted sample can be used for up to 2 hours at room temperature. Alternatively, non-citrated whole blood (native blood TEG or NATEM) can be used, but it must be tested immediately. The test and reagents used should be at room temperature. To perform the test, 340 uL of citrated blood is pipetted into the study cup, then recalcified by adding 20 uL of 0.2M calcium chloride, followed by activation with a kaolin-cephalin reagent. Kaolin, a negatively charged molecule primarily composed of hydrated aluminum silicate, activates Factor XII, initiating the intrinsic coagulation pathway. Accurate and reproducible TEG results depend on precise proportioning of the blood and kaolin-cephalin reagent.[47]

Picture 2: TEG Analysis



TEG® Hemostasis Analyzer Tracing Image and TEG® LY30 Clot Breakdown Diagram reproduced from Haemonetics Corporation. TEG® and Thromboelastograph® are registered trademarks of Haemonetics Corporation in the US, other countries, or both. Graphic 80241 Version 4.0

Picture 3: TEG Interpretation [48]

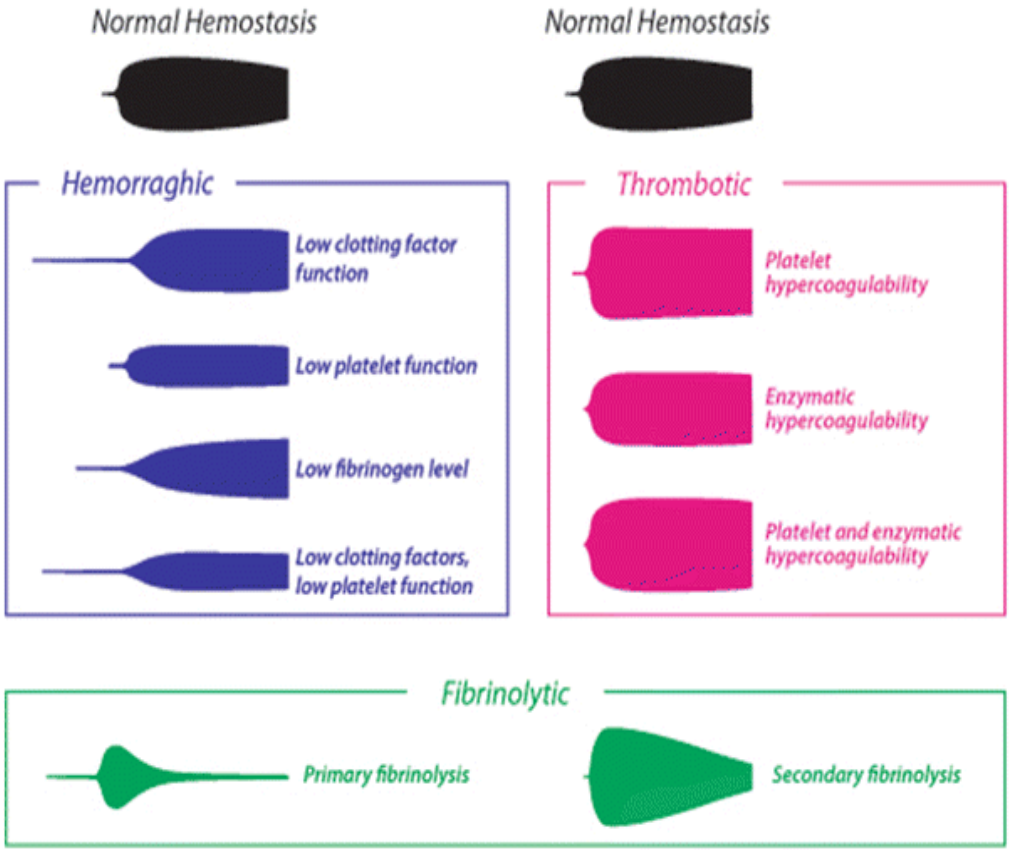


Table B: TEG Parameters [38,39,49]

Components	**Definition**	**Normal Values**	**Problem with**	**Treatment**
R Time	Time to start forming clot	5-10 minutes	Coagulation Factors	FFP
K Time	Time until clot reaches a fixed strength	1-3 minutes	Fibrinogen	Cryoprecipitate
Alpha Angle	Speed of fibrin accumulation	53-72 degrees	Fibrinogen	Cryoprecipitate
Maximum Amplitude (MA)	Highest vertical amplitude of the TEG	50-70 mm	Platelets	Platelets
Lysis at 30 minutes (LY30)	Percentage of amplitude reduction 30 minutes after maximum amplitude	0-8%	Excess fibrinolysis	Tranexemic Acid and/or Aminocapric Acid

Table C: Types of TEG[44,45]

TEG	ACTIVATOR	COMMENT
Native TEG	None	Most sensitive
Conventional TEG	Kaolin	Activated clotting cascade
Rapid TEG	Tissue factor+kaolin	Gives rapid result
Heparinase TEG	Heparinase	Presence of heparin is indicated ,when this TEG improved clotting compared to other TEG

CCT AND TEG

In patients with CLD strong correlation has been observed between TEG measures of clot formation and clot strength and conventional fibrinogen level. As opposite to this a, weak or unpredictable correlations exist between TEG and CCTs in measuring coagulation initiation (i.e. TEG R-time and PT/INR/aPTT), TEG and conventional platelet count, and measures of fibrinolysis (TEG LY30 and traditional D-dimer[6,50,51]. This occurs due to the use of different activators, the use of whole blood or plasma. The R-time, unlike INR, reflects the balance of both pro- and anticoagulant factors.

A stressful condition (surgery/sepsis) causes the release of endogenous glycosaminoglycans (GAGs) (e.g., heparin sulfate and dermatan sulfate) from the endothelium glycocalyx layer or mast cell, which, when shed, retain their anticoagulant activity.[52,53] They act as endogenous heparin and prevent spontaneous thrombosis in the progressively procoagulant microvasculature seen in these conditions. A study by **Senzolo et al**. illustrated GAGs affected hemostasis in cirrhotic patients with sepsis and thus can increase the risk of bleeding.[54] Another prospective analysis demonstrated the presence of these endogenous heparins in patients with cirrhosis and acute variceal bleeding and was found to be associated with bleeding-related mortality.[55] After treatment, these endogenous heparinoids are cleared from the circulation, and the coagulation profile

gets normalized. This highlights the association between the inflammation pathway and coagulation cascade.

The native TEG is highly sensitive to the presence of heparin and heparin-like substances, which can be detected by an increased R-time on TEG analysis.[56] CCTs are insensitive to this effect. However, adding heparinase I, which cleaves heparin-like compounds, can demonstrate a heparin-like effect due to elevated GAGs, correlating with anti-Xa activity.[57] Therefore, heparinase-modified TEG will normalize the prolongation of the R-value observed with native TEG, helping to differentiate between anticoagulation factor deficiency and heparin-induced coagulopathy by employing heparinase-modified TEG and the native TEG.

The risk of developing VTE is similar in cirrhotic and non-cirrhotic patients.[29,35] Hypercoagulability is seen on TEG as shortened R or K or enhanced clot strength (MA), or a combination of both. **Huang et al.** observed a significantly shorter R in cirrhosis with non-malignancy PVT.[58] **Zanetto et al.** found that elevated MA was associated with PVT in cirrhotic patients with hepatocellular carcinoma.[59]

A well-recognized, potentially fatal complication of LT, associated with high mortality – acute intracardiac thrombi and PE are rare. **Krzanicki et al.** demonstrated that a hypercoagulable state is quite common during liver transplantation.[60] TEG showed hypercoagulability in >70% of TE in orthotopic LT.[61] Hypercoagulable TEG patterns correlated well with the formation of intracardiac thrombi. The risk of thrombosis can be seen on rapid TEG (after 5 or 10 min of clotting time)as an increase in the MA. The clinical importance of hypercoagulability on TEG during LT is yet to be recognized. Hence, it would appear unreasonable to transfuse blood products or avoid anticoagulants based on raised CCTs when a hypercoagulable state is seen on TEG.

A systematic review and meta-analysis of 5 randomized controlled trials compared thromboelastography (TEG)-guided hemostatic management with conventional coagulation tests (CCT).[62] The study focused on primary outcomes, such as the use of blood products like fresh frozen plasma (FFP) and platelet units, as well as secondary outcomes, including

mortality, transfusion-related adverse events, excessive bleeding events, and duration of intensive care unit (ICU) stay.

The results revealed a significant fivefold reduction in platelet use with thromboelastography compared to the control, with a relative risk of 0.17 (95% CI: 0.03–0.90; p = 0.04). However, there was no notable difference in the use of FFP. Thromboelastography was linked to a marked decrease in overall blood product usage (p < 0.001), including combined FFP and platelets (p < 0.001) and cryoprecipitate (p < 0.001). While there were no significant differences in bleeding rates or long-term mortality between the groups, the thromboelastography-guided approach showed lower mortality at 7 days compared to the control, with a relative risk of 0.52 (95% CI: 0.30–0.91; p = 0.02).

These findings indicate that implementing thromboelastography-guided therapy in cirrhotic patients may improve blood management by reducing the need for blood products without increasing bleeding complications.

Tangcheewinsirikul et al. found that thromboelastography significantly reduced the need for platelet and cryoprecipitate transfusions. Specifically, they reported a 48% lower rate of FFP transfusion in the TEG group compared to controls (relative risk [95% CI] p = 0.001 [63]).[63]

Similarly, **Kovalic et al.** noted a significant reduction in platelet and FFP transfusion requirements with thromboelastography compared to standard laboratory test-guided therapy, with pooled odds ratios of 0.29 (95% CI; p = 0.009) and 0.19 (95% CI p < 0.00001), respectively.[64] They also observed a significant decrease in overall bleeding events and intraoperative bleeding during liver transplantation when using thromboelastography compared to standard laboratory test-based care. However, there was no significant difference in mortality between the groups.

De Pietri et al. conducted a randomized prospective trial comparing TEG-guided blood product use with traditional standard methods. Their study demonstrated that TEG-guided transfusion significantly reduced the need for transfusions without increasing bleeding complications.[38]

Kumar et al. conducted another randomized controlled trial, assessing 96 cirrhotic patients with nonvariceal bleeding.[65] The patients were divided

into a TEG-guided transfusion strategy group and a standard coagulation-based transfusion group. The TEG-guided group received significantly fewer blood product transfusions and experienced fewer adverse transfusion-related events.

The 2019 American Gastroenterological Association (AGA) clinical practice update on coagulation in cirrhosis suggests that thromboelastography could play a role in assessing clotting in cirrhosis patients in the future, but currently there are no validated target levels for it.[66] According to the 2020 Society of Critical Care Medicine (SCCM) guidelines for managing critically ill adults with acute and acute-on-chronic liver failure undergoing procedures, there is conditional guidance for using thromboelastography instead of measuring INR, platelet, and fibrinogen.[67] Additionally, recent guidance on periprocedural hemostatic management in cirrhosis patients by the Scientific and Standardization Committee/International Society on Thrombosis and Hemostasis (SSC/ISTH) mentions a potential role for thromboelastography.[68]

MATERIAL AND METHODS

Study design and setting

This was a prospective observational study conducted in the Departments of General Medicine, Gastroenterology, Cardiology, Surgery and Intervention Radiology at Dayanand Medical College and Hospital, Ludhiana, between 15th September 2022 to 31st December 2022 and 1st July 2023 to 31st December 2023.All patients with cirrhosis who were scheduled to undergo invasive procedures were screened and those who had coagulopathy (as defined by CCTs) were included in the present study. Patients meeting the inclusion criteria and giving consent underwent TEG and TEG guided transfusion of blood products. Intra and post procedural complications were recorded.

The invasive procedures being performed can be classified on basis of bleeding risk into two categories [38]:-

1. Low Risk of bleeding (bleeding risk <3%)

- Paracentesis
- Thoracentesis
- Central venous cannulation
- Transjugular intrahepatic portosystemic shunt (TIPSS)

2. High risk of bleeding(>3%)

- Endoscopic variceal banding
- Ablative and non-surgical therapies for Hepatocellular carcinoma
    - Radiofrequency ablation (RFA)
    - Percutaneous Ethanol Injection (PEI)
    - Transarterial radioembolization (TARE)
    - Transarterial chemoembolization (TACE)
- Percutaneous biopsy from any site
- Drainage of abscesses or collections
- ERCP with sphincterotomy

Cirrhosis of the liver was characterized by liver scarring that leads to impaired liver function due to chronic liver damage.[69] On ultrasonography, cirrhosis appears as surface irregularity, coarse echotexture, a reduced right lobe to caudate lobe ratio, and signs of portal

hypertension.[70] Transient elastography shows liver stiffness over 14 kPa indicating cirrhosis, with values over 21 kPa linked to portal hypertension and its complications.[71,72] Histologically, cirrhosis is marked by fibrotic septa connecting portal tracts and central veins, creating hepatocyte islands without a central vein.[73]

Coagulopathy in patients with cirrhosis was defined as prolonged prothrombin time (>12.6) , elevated international normalized ratio of the prothrombin time (PT/INR) >1.5 ,low fibrinogen levels, and low platelet counts <50x 10^3/µl.[74]

Clinically significant post-procedure bleeding was defined as any bleeding requiring blood transfusions additional and unexpected hemostatic measures , hospitalization for patients in whom the procedure was carried out as outpatients and bleeding related extension of hospital stay.[11]

PATIENTS:

All patients with cirrhosis who were scheduled for invasive procedures and had coagulopathy (as defined by CCTs, i.e. INR > 1.5 or platelet count <50x10^3/µl) were screened and included.

INCLUSION CRITERIA

1. Age >18yrs
2. Diagnosis of cirrhosis documented by clinical or imaging (USG/fibroscan) or liver biopsy
3. Presence of coagulopathy according to conventional coagulation tests defined as INR > 1.5 or patients with Platelet <50x10 ^{3}/ul.
4. Undergoing invasive procedure like ascitic tap /pleural tap (paracentesis) ,percutaneous drainage of abscesses, collections, central line insertion ,dialysis catheter insertion ,coronary angiography, PTCA, surgical procedure like biopsy from various sites ,debridement ,ERCP with sphincterotomy, treatment of HCC like percutaneous alcohol injection, transarterial chemoembolization (TACE), or transarterial radioembolization (TARE).

EXCLUSION CRITERIA

- Patient without clinical/imaging evidence of cirrhosis
- Ongoing bleeding

- Current thrombotic events (arterial/venous clot)
- Antiplatelet or coagulant therapy at time of enrollment
- Hemodialysis in the previous seven days
- Patient with primary bleeding disorder/ bone marrow disorder
- Patient with any blood transfusion during hospitalization before TEG
- Hypercoagulable state like Polycythemia vera
- Chronic kidney disease
- Pregnancy
- Sepsis
- DIC

SAMPLING :

Blood samples (1-3 ml) were obtained using the double-syringe technique from a clean venipuncture at the antecubital fossa. Whole blood 1 ml was transferred into kaolin vial and gently inverted 5 times. Immediately 360ul of blood sample was pipetted from kaolin vial into cup and test was started for results .

The TEG was done using a TEG Hemostasis Analyzer model 5000 (Haemonetics Company). Clot formation was triggered by contact activation without the addition of activators. The specific TEG variables used to guide blood component transfusions were R time, alpha angle, and MA.

Table D: Indication of Transfusion as per TEG[75]

1 Single Donor Platelet Unit (SDP) equals 5 Random Donor Platelet Unit (RDP) [76]

TEG RESULT	**TREATMENT**
R > 14 mins	4 UNITS OF FFP
MA ≤ 40 mm	1 Single Donor Platelet Unit (SDP)
ANGLE < 45 degrees	0.06 units/kg cryoprecipitate

One unit of FFP – 250 ml/unit

One unit of cryoprecipitate- 20-40 ml/unit

One unit of SDP – 200 ml/unit

One unit of RDP – 100 ml/unit

Conventional coagulation tests are laboratory tests used to evaluate the blood's ability to clot properly. The main conventional coagulation tests include.[77]

1. Prothrombin Time (PT) - Measures the time it takes for plasma to clot when exposed to a tissue factor.

- Assesses the extrinsic and common coagulation pathways.
- Often reported as an International Normalized Ratio (INR) for standardization.

2. Activated Partial Thromboplastin Time (aPTT) - Measures the time it takes for plasma to clot when exposed to a surface activator.

- Assesses the intrinsic and common coagulation pathways.

3. Thrombin Time (TT) - Measures the time it takes for plasma to clot after the addition of thrombin.

- Assesses the final step of the coagulation pathway, the conversion of fibrinogen to fibrin.

4. Fibrinogen Level- Measures the amount of fibrinogen, a protein necessary for clot formation, in the blood.

5. Platelet Count - Measures the number of platelets in the blood, which are essential for clot formation.

6. D-dimer Test - Measures the amount of D-dimer, a protein fragment produced when a blood clot dissolves.

- Used to assess thrombotic disorders and the presence of an abnormal clotting process.

Table E: Indication of transfusion as per CCT[78-82]

CCT RESULT	TREATMENT
PT/INR >1.5	FFP at dose 15ml/kg ideal body weight
PLATELETS <50X 10^3/µl	1 Single Donor Platelet Unit (SDP)

In patient with ascites, for better standardization ,the amount of blood products administered in patients shall be calculated according to ideal body weight of the patient using the Devine formula as follows:- [38]

Male ideal body weight = 50 Kg + 2.3 Kg per inch over 5 feet

Female ideal body weight = 45.5 kg + 2.3 Kg per inch over 5 feet

Table F: Grading of ascites as defined by International Ascites Club [83]

Grade of Ascites	
Grade 1 (mild)	Ascites is only detectable by ultrasound examination.
Grade 2 (moderate)	Ascites causing moderate symmetrical distension of the abdomen.
Grade 3 (large)	Ascites causing marked abdominal distension

- Grading of hepatic encephalopathy was based on West Haven Criteria [84]

Table G: Child Pugh score[85]

FACTOR	UNITS	POINT 1	POINT 2	POINT 3
Serum Bilirubin	mg/dl	<2	2-3	>3
Serum albumin	g/dl	>3.5	3-3.5	<3
PT/INR		<1.7	1.7-2.3	>2.3
Ascites		none	Easily controlled	Poorly controlled
Encephalopathy		none	Minimal	advanced

Child Pugh Score ranges between 5-15

Child Pugh Class A - 5-6 score

Child Pugh Class B - 7-9 score

Child Pugh Class C - ≥10 score

- Model for end-stage liver disease (MELD) score [86] is calculated by the given formula (9.57 × loge (creatinine) + 3.78 × loge (total bilirubin) + 11.2 × loge (INR) + 6.43.

SAFETY

At the end of the procedure, patients were reassessed daily for 5days or until discharge. Any clinically significant bleeding was recorded, in the case of transfusion, amount of blood and transfusion-related side effects were noted.

STATISTICAL ANALYSIS

Obtained data were presented as a mean ± standard deviation, ranges, median(IQR), numbers and percentage according to requirement. Results were analyzed using Wilcoxon; ranked test for unrelated data (Z-Test) and Chi-square test (χ test). All statistical calculations were done using SPSS (Statistical Package for the Social Science) SPSS 21.0 version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows. $P < 0.05$ was considered statistically significant.

OBSERVATION AND RESULTS

Table 1: Demographic, Clinical, biochemical characteristics of patients enrolled.

Parameters	Values
Age, year Mean ±SD	50.56 ± 11.71
Male n, (%)	90 (92.8)
Ideal body weight ,kg, Mean± SD	64.55 ± 8
Etiology n (%) HCV Alcohol related Autoimmune related Metabolic associated steatotic liver disease (MASLD)	 1 (1.0) 78 (80.4) 3.1 (3.1) 15 (15.5)
Ascites grade ≥ 2 n (%)	66 (68.04)
HE grade > 1 n (%)	45 (46.39)
HCC n (%)	3 (3.1)
MELD score ,Mean ±SD	24.80 ± 8.45
Child Pugh Score Class n(%) A B C	 4 (4.1) 15 (15.5) 78 (80.4)
INR Mean ± SD	2.78 ± 1.14
Platelet count 10^3/µL Mean ± SD	86.82 ±76.83
WBC,10^9/L ,Mean ± SD	10.47 ± 7.49
Pre procedure Hemoglobin, g/dl ,Mean ±SD	9.70 ± 1.45
TEG Parameters R (min) Mean ± SD Alpha angle (degree)Mean ± SD Maximum amplitude (mm) Mean ± SD	 5.11 ± 2.76 52.69 ± 14.26 40.93 ± 12.06

Observation: Among the 97 patients with chronic liver disease and coagulopathy who underwent invasive procedures, the majority were male (92.8%) and in Child-Pugh class C (80.4%). The average age was 50.56 years, with a mean platelet count of 86.82 x 10^3/µl and a PT/INR of 2.78. The mean TEG values were an R time of 5.11 minutes and an MA value of 40.93 mm. Additionally, 68.04% of patients had ascites grade ≥2, and 46.39% had encephalopathy greater than grade 1.

Table 2: Etiology of cirrhosis

ETIOLOGY	No. of cases	Percentage
Alcoholic Liver Disease	78	80.4%
Metabolic associated steatotic liver disease (MASLD)	15	15.5%
Autoimmune Liver Disease	3	3.1%
Hepatitis C	1	1.0%
Total	97	100.0%

Observation: The most common etiology of CLD among selected patients was Alcoholic liver disease (80.4%) followed by metabolic associated steatotic liver disease (15.5%). Autoimmune liver disease was seen in 3% patients. HCV was the cause of CLD IN 1%.

Figure 1: Etiology of CLD

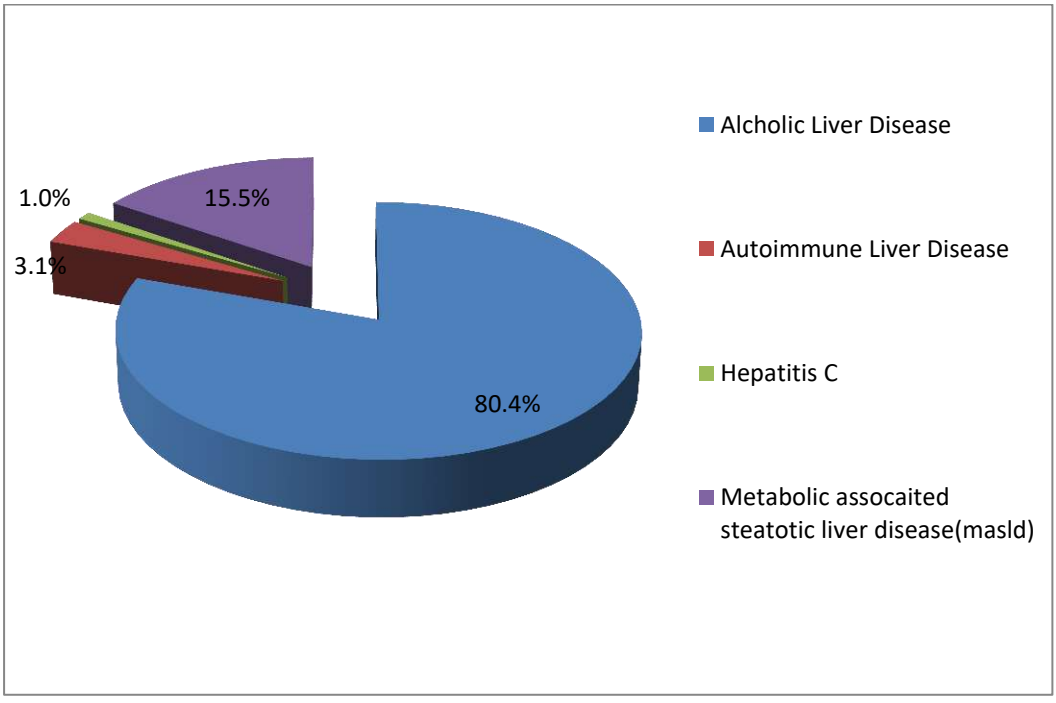


Table 3: Distribution of procedures

RISK OF BLEEDING	No. of cases	Percentage
high	35	36.1%
low	62	63.9%
Total	97	100.0%

Observation: Among 97 patients, 63.9%patients (n= 62) underwent procedures with low risk of bleeding and 36.1% patients (n= 35) underwent procedure with high risk of bleeding.

Figure 2: Distribution of procedures

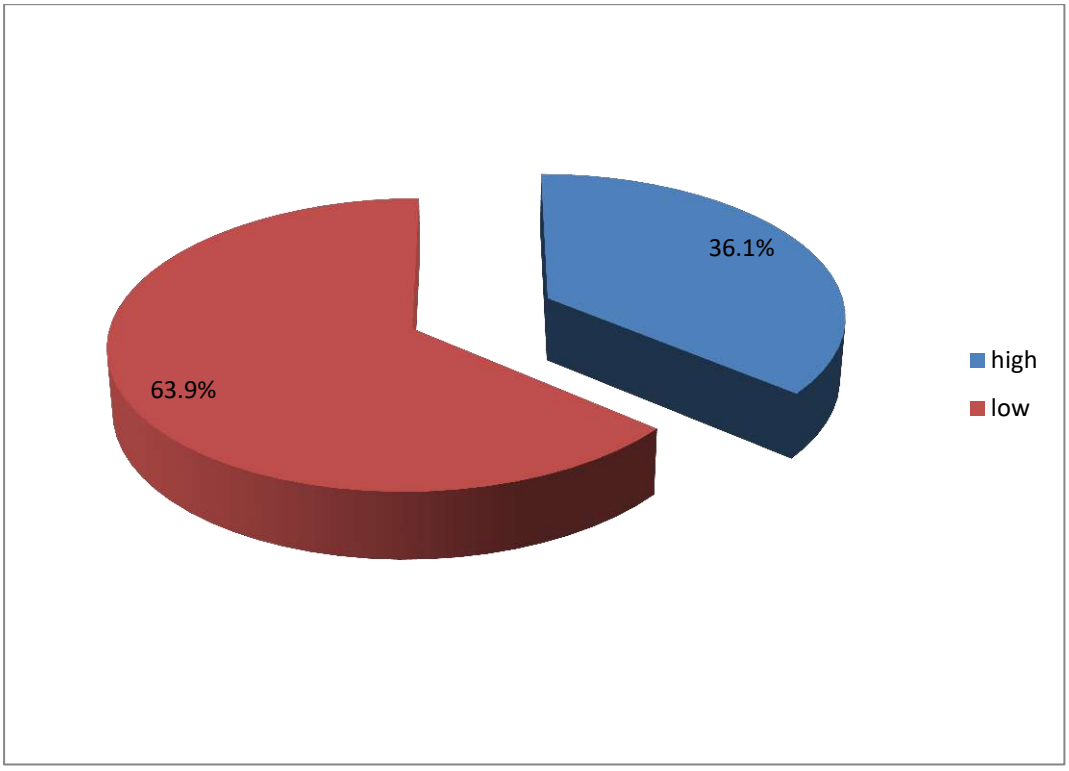


Table 4: Distribution of procedures as low / high risk of bleeding

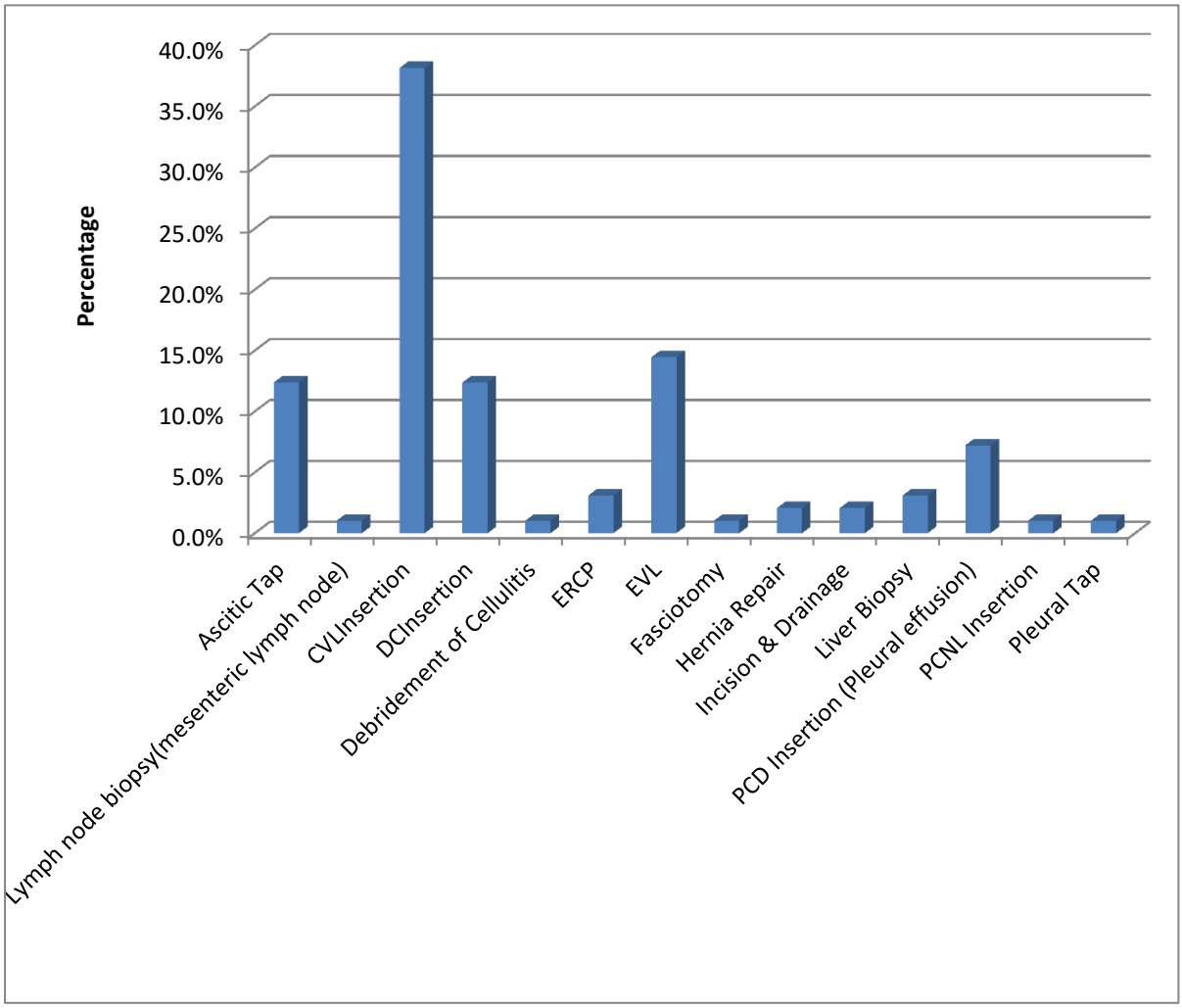
LOW RISK	**Number (n)**	**Percentage (%)**
Ascitic Tap	12	12.4
CVC Insertion	37	38.1
Pleural tap	1	1
DC Insertion	12	12.4
High RISK	**Number (n)**	**Percentage (%)**
EVL	14	14.4
Liver Biopsy	3	3.1
Lymph node biopsy (mesenteric lymph node)	1	1
ERCP	3	3.1
Hernia Repair	2	2.1
Debridement of cellulitis	1	1
Incision and drainage	2	2.1
Fasciotomy	1	1
PCD insertion	7	7.2
PCNL Insertion	1	1

CVC: Central Venous catheter /DC -Dialysis catheter /ERCP-Endoscopic retrograde cholangiopancreatography/ EVL – Endoscopic variceal ligation/ PCD - Percutaneous drainage /PCNL - Percutaneous Nephrolithotomy

Observation: The most common low risk procedure was central venous line insertion done in 38.1% followed by dialysis catheter insertion (12.4%), ascitic tap (12.4%)and pleural tap (1%).

The most common high risk procedure was endoscopic variceal ligation (14.4%) followed by percutaneous drainage insertion (7.2%), liver biopsy, biopsy from other site(mesenteric lymph node), debridement of cellulitis, ERCP, hernia repair , incision &drainage and fasciotomy

Figure 3: Distribution of procedures as low / high risk of bleeding



.Table 5: Comparison of utilization of blood products as per TEG in relation CCTs (n=97).

	TEG		CCT		Chi-square value	p-value
	No. of cases	Percentage	No. of cases	Percentage		
FFP only	0	0.0%	51	52.6%	11.681	0.001
SDP only	42	43.3%	4	4.1%		
Both	1	1.0%	42	43.3%		
Total	43	44.3%	97	100.0%		

Observation: Using TEG, only FFP were transfused none of the patient (0%) v/s 51 patients needed only FFP as per CCTs (52.6%) (p value <0.001).Only SDP were transfused in 42 patients as per TEG (43.3%) however, only Platelet (SDP) were required in 4 patients (4.1%). Only one patient was transfused both FFP and platelet unit as per TEG (1.0%).However 42 patients would have been transfused as per CCTs (43.3%) (p value <0.001).

Figure 4: Comparison of utilization of blood products as per TEG in relation CCTs (n=97).

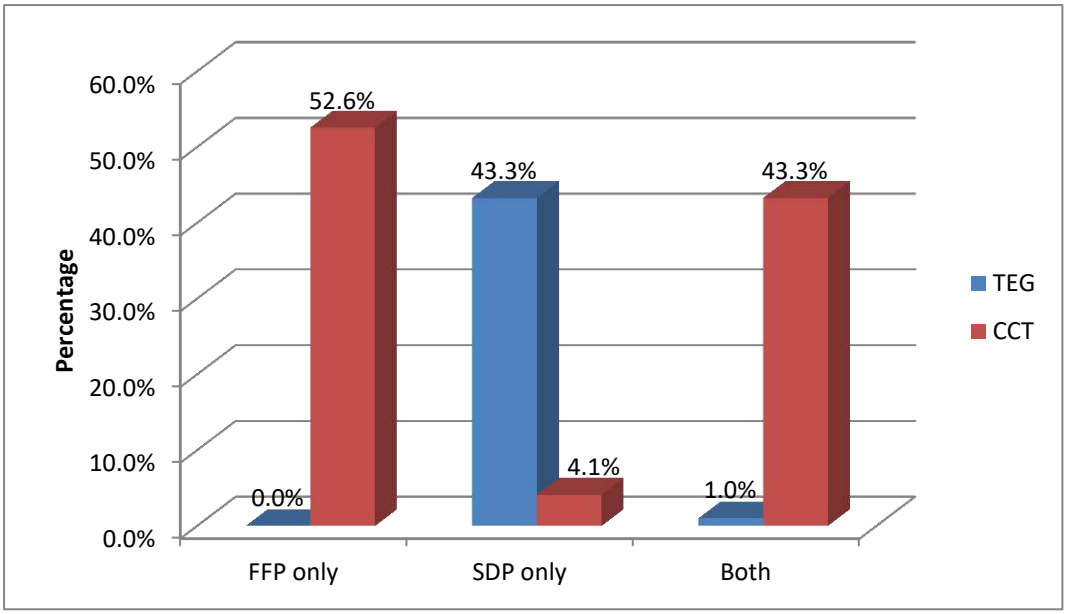


Table 6: Comparison of utilization of blood products as per TEG in relation to CCTs among patients who underwent low risk procedures (n=62).

LOW	TEG		CCT		Chi-square value	p-value
	No. of cases	Percentage	No. of cases	Percentage		
FFP only	0	0.0%	23	37.1%	81.784	0.001
PLT	32	51.6%	3	4.8%		
Both	0	0.0%	36	58.1%		
Total	32	51.6%	62	100.0%		

Observation: Among patients undergoing low risk procedure (n=62), using TEG, only FFP were transfused none of the patient (0%) v/s 23 patients needed only FFP as per CCTs (37.1%) (p value <0.001). Only platelet unit were transfused in 32 patients as per TEG (51.6%) however, only platelet unit were required in 3 patients (4.8%). None patient was transfused both FFP and platelet unit as per TEG (0%). However 32 patients would have been transfused both FFP and platelet unit as per CCTs (58.1%) (p value <0.001).

Figure 5: Comparison of utilization of blood products as per TEG in relation to CCTs among patients who underwent low risk procedures (n=62).

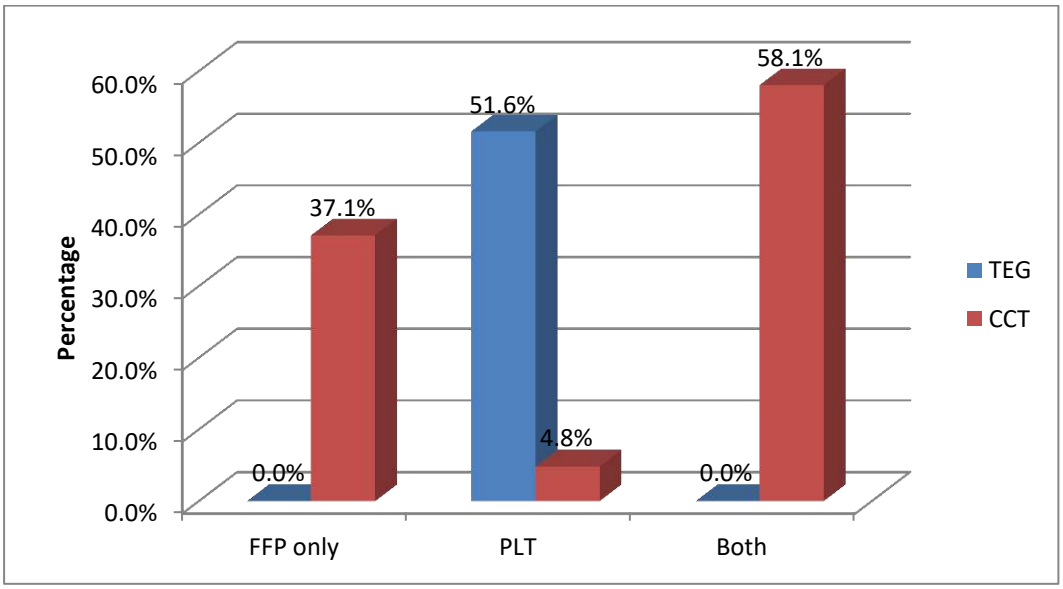


Table 7: Comparison of utilization of blood products as per TEG in relation to CCTs among patients who underwent high risk procedures (n=35)

HIGH	TEG		CCT		Chi-square value	p-value
	No. of cases	Percentage	No. of cases	Percentage		
FFP only	0	0.0%	28	80.0%	36.293	0.001
PLT	10	28.6%	1	2.9%		
Both	1	2.9%	6	17.1%		
Total	11	31.4%	35	100.0%		

Observation: Among patients undergoing high risk procedure (n=35), using TEG, only FFP were transfused none of the patient (0%) v/s 28 patients needed only FFP as per CCTs (80.0%)(p value <0.001).Only platelet unit were transfused in 10 patients as per TEG (28.6 %) however, only platelet unit were required in 1 patients (2.9%).One patient was transfused both FFP and platelet unit as per TEG (2.9%). However 6 patients would have been transfused both FFP and platelet unit as per CCTs (17.1%) (p value <0.001).

Figure 6: Comparison of utilization of blood products as per TEG in relation to CCTs among patients who underwent high risk procedures (n=35)

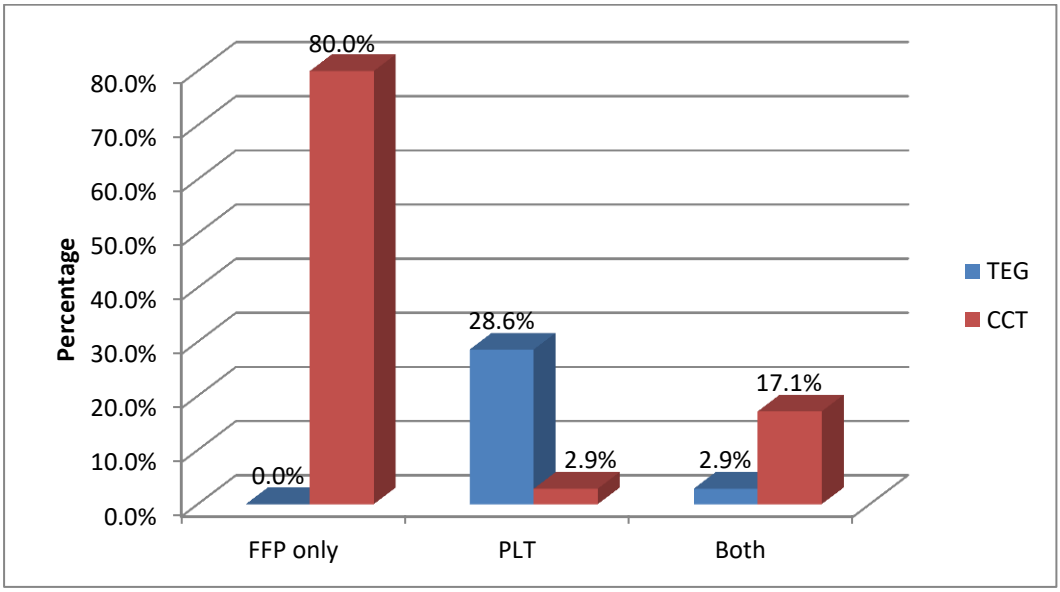


Table 8: Comparison of volume of FFP transfused per patient as per TEG in relation CCTs

FFP transfused, mL/patient	TEG		CCT		Z	p-value
	Mean	SD	Mean	SD		
LOW	0.00	0.00	943.55	276.91	26.830	0.001
HIGH	28.57	169.03	950.00	225.24	19.726	0.001
Total	10.31	101.53	945.88	258.27	33.449	0.001

Observation: The volume of FFP transfused per patient (that is mean) using TEG in patient who underwent low risk procedure was 0ml which was significantly lower than the amount requirement expected with CCT that is 943.55ml ($p<0.001$). The similar observation was seen in patients who underwent high risk procedures (28.57ml v/s 950.0ml $p<0.001$). Overall 10.31ml FFP were transfused per patient using TEG which is significantly lower than 945.88ml FFP requirement predicted as per CCTs.

Figure 7: Comparison of volume of FFP transfused per patient as per TEG in relation CCTs

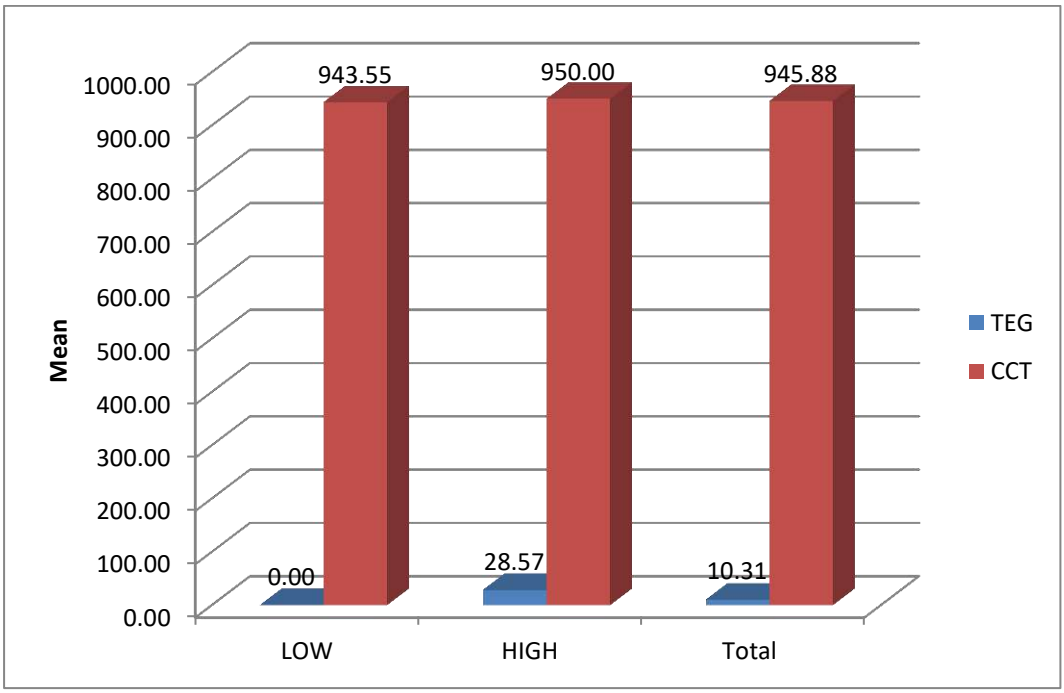


Table 9: Comparison of transfusion of FFP as per TEG in relation to CCTs among patients who underwent low risk procedure.

LOW	TEG		CCT		p-value
n=62	No. of cases	Percentage	No. of cases	Percentage	
FFP	0	0.0%	59	95.2%	0.001

Observation: Among patients who underwent low risk procedures (n=62) none of the patient was transfused FFP (0%). On the other hand, 59 patients that is 95.2% needed FFP transfusion as per CCTs (p<0.001).

Figure 8: Comparison of transfusion of FFP as per TEG in relation to CCTs among patients who underwent low risk procedure.

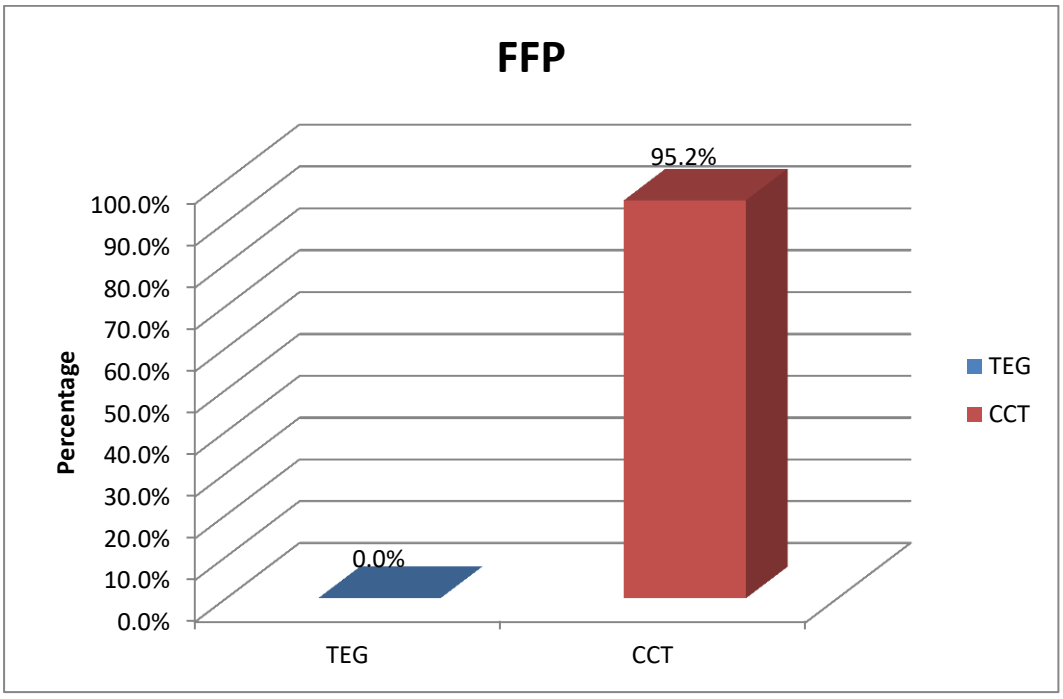


Table 10: Comparison of transfusion of FFP as per TEG in relation to CCTs among patients who underwent low risk procedure

HIGH	TEG		CCT		p-value
n=35	No. of cases	Percentage	No. of cases	Percentage	
FFP	1	2.9%	34	97.1%	0.001

Observation: Among patients who underwent high risk procedures (n=35) one patient was transfused FFP (2.9%). On the other hand, 34 patients that is 97.1% needed FFP transfusion as per CCTs (p<0.001).

Figure 9: Comparison of transfusion of FFP as per TEG in relation to CCTs among patients who underwent low risk procedure.

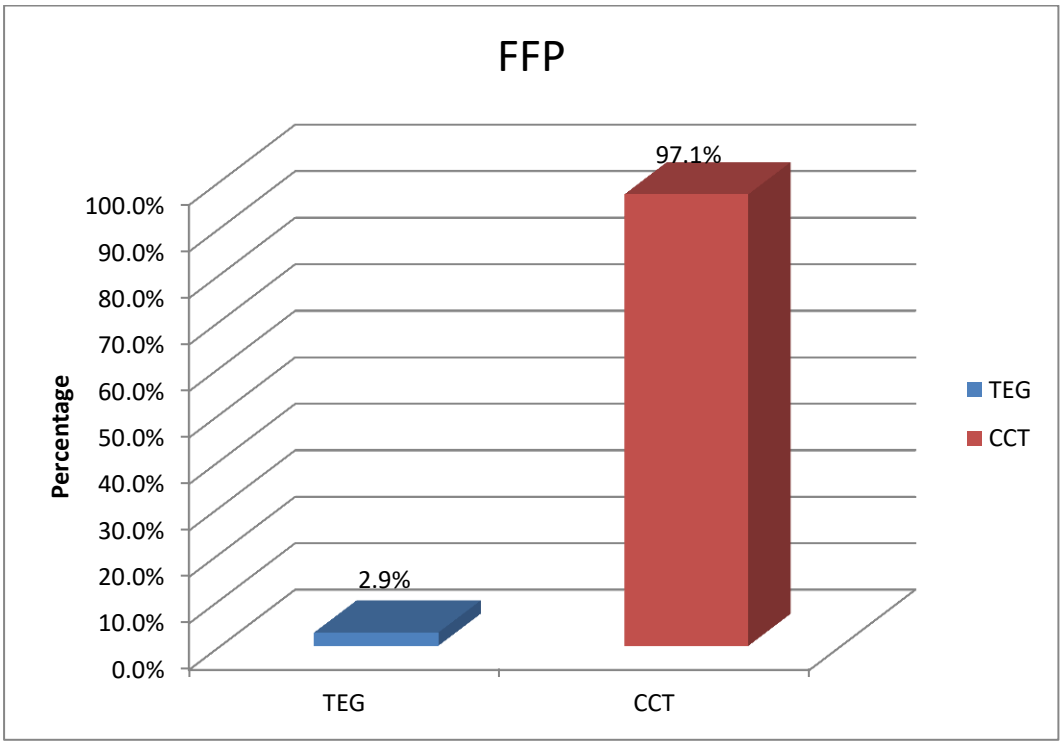


Table 11: Comparison of total amount of FFP transfused (ml) as per TEG in relation to CCTs

	TEG	CCT	p-value
FFP Infused (ml)	Total	Total	
Low	0	58500	0.001
High	1000	33250	0.001
Total	1000	91750	0.001

Observation: The total amount of FFP transfused using TEG in patients who underwent low risk procedure was 0ml which was significantly lower than the amount requirement expected with CCT that is 58500ml ($p<0.001$). The similar observation was seen in patients who underwent high risk procedures (1000ml v/s 33250ml $p<0.001$). Overall only 1000ml FFP were transfused using TEG which is significantly lower than 91750ml FFP requirement predicted as per CCTs ($P<0.001$)

Figure 10: Comparison of total amount of FFP transfused (ml) as per TEG in relation to CCTs

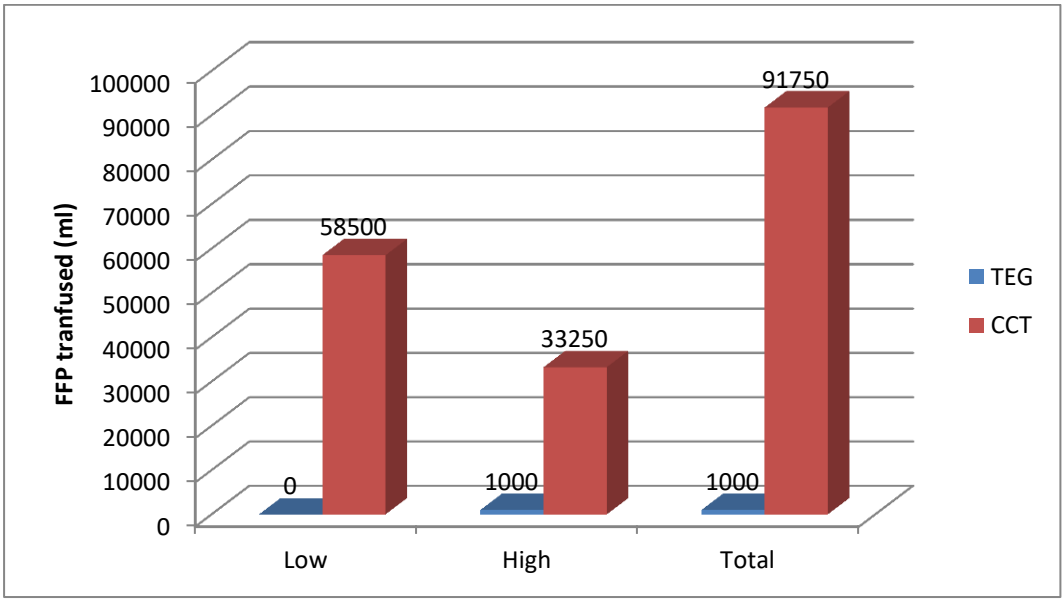


Table 12: Comparison of platelet utilization as per TEG in relation to CCTs

n=97	TEG		CCT		p-value
PLTs Infused, Units	No. of cases	Percentage	No. of cases	Percentage	
1SDP	43	44.3%	46	47.4%	0.664

Observation: Among 97 patients, 43 patients had MA <40 mm and hence were given platelet unit (1SDP) (44.3%). As per CCT among 97 patients, 46 patients had platelet count lesser than 50 x 10^3/ul and hence would have required platelet transfusion (47.4%). This difference is not statistically significant.

Figure 11: Comparison of platelet utilization as per TEG in relation to CCTs

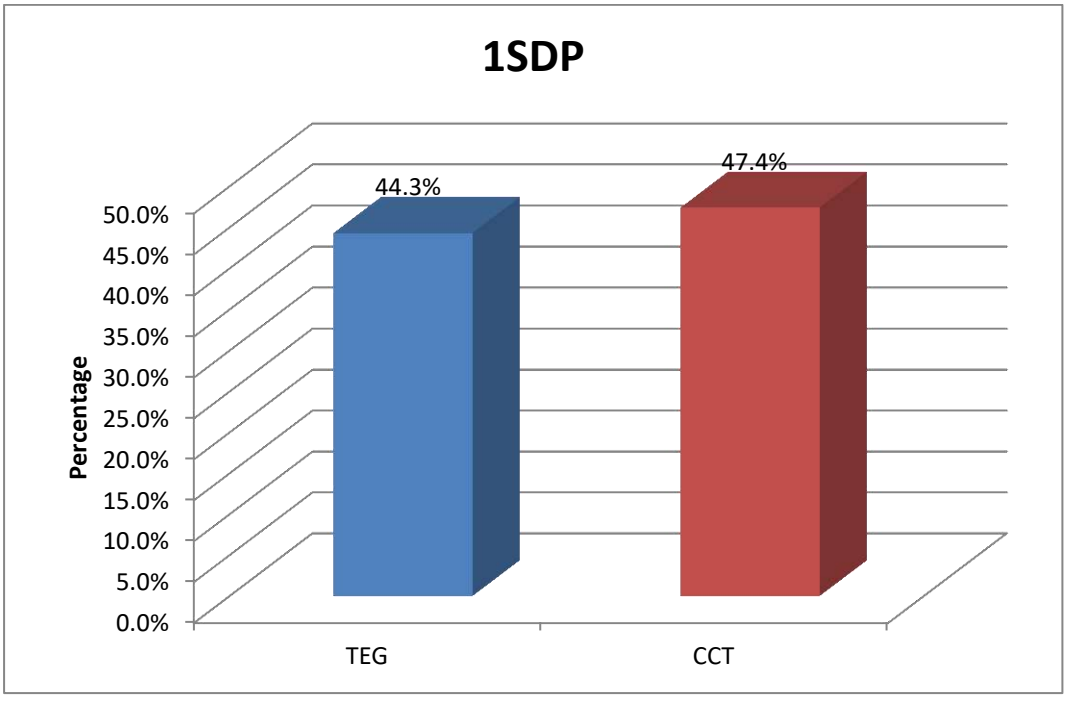


Table 13: Comparison of platelet utilization as per TEG in relation to CCTs among patients who underwent low risk procedures.

LOW, n=62	TEG		CCT		p-value
PLTs Infused, Units	No. of cases	Percentage	No. of cases	Percentage	
1SDP	32	51.6%	39	62.9%	0.206

Observation: Among 62 patients who underwent low risk procedure, 32 patients were given platelet unit in view of MA <40 mm as per TEG results (51.6%). However out of 62 patients 39 patients had platelet less than 50 $x10^3$/ul. This difference is not statistically significant.

Figure 12: Comparison of platelet utilization as per TEG in relation to CCTs among patients who underwent low risk procedures

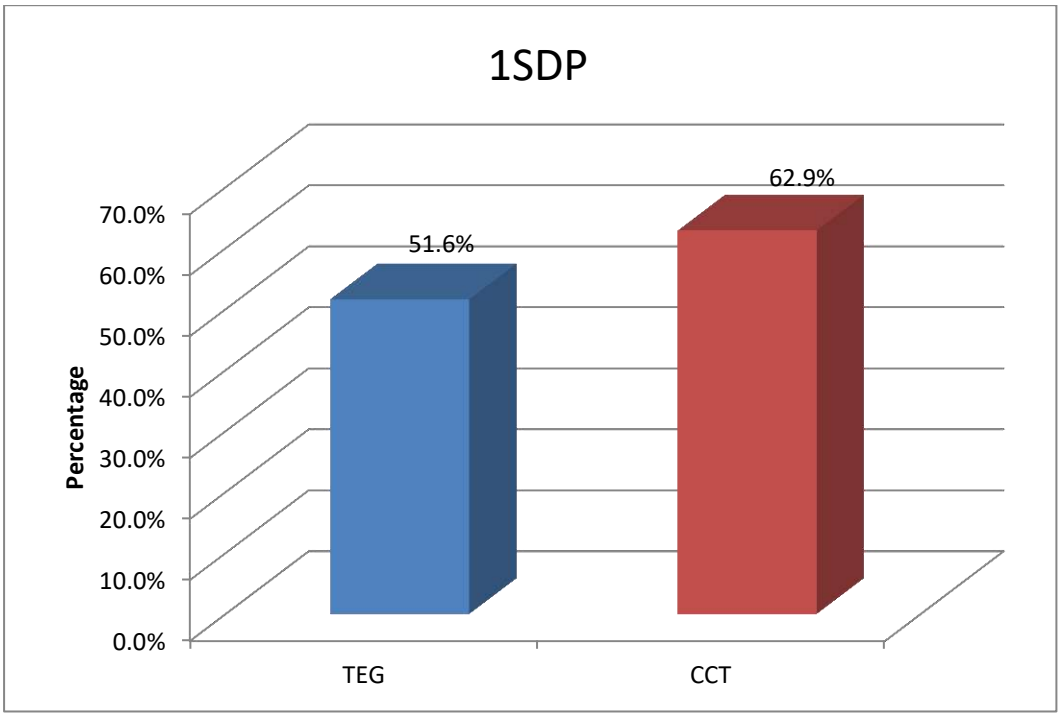


Table 14: Comparison of platelet utilization as per TEG in relation to CCTs among patients who underwent high risk procedures

HIGH, n=35	TEG		CCT		p-value
PLTs Infused, Units	No. of cases	Percentage	No. of cases	Percentage	
1SDP	11	31.4%	7	20.0%	0.277

Observation: Among 35 patients who underwent high risk procedure, only 11 patients had platelet count <50 x10^3/ul (20.0%) however as per TEG results MA value <40mm was seen in 11 patients and were transfused platelet unit (31.4%). This indicated that platelet count is not a true indicator of platelets in cirrhosis.

Figure13: Comparison of platelet utilization as per TEG in relation to CCTs among patients who underwent high risk procedures

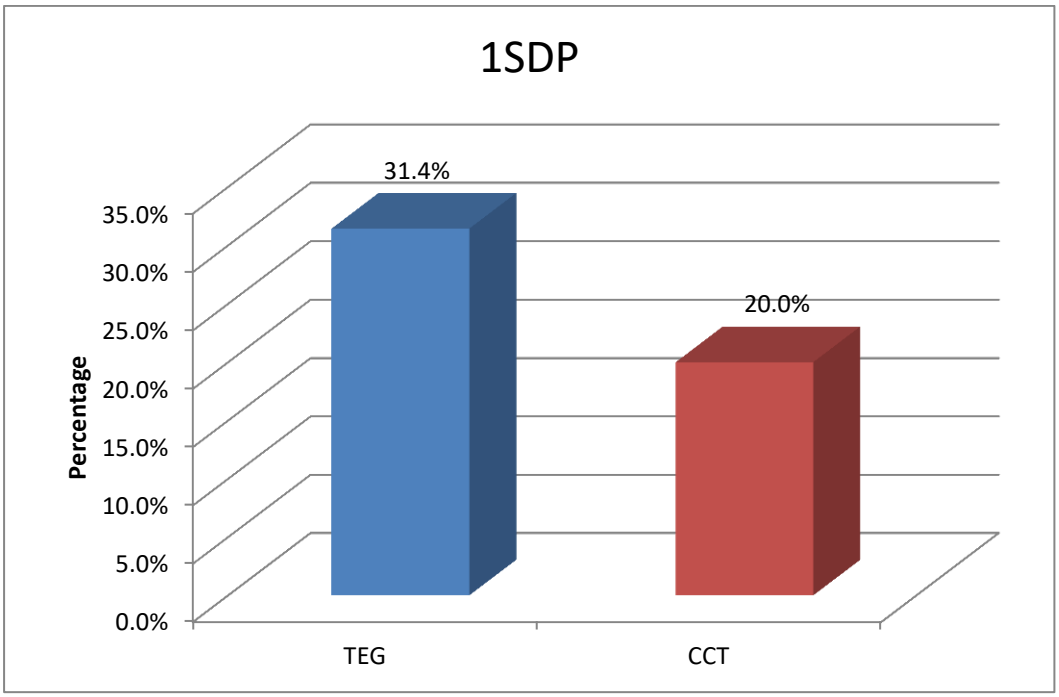


Table 15: Comparison of cost spent on transfusion of blood products as per TEG in relation to CCTs.

	TEG		CCT		Z	p-value
	Mean	SD	Mean	SD		
Total cost of transfusion in Rs.	5679.38	6415.85	10562.89	6192.57	6.408	0.001
Net Cost in Rs.	10779.38	6415.85	11369.18	7401.09	0.715	0.476

Observation: The total money spent on transfusion per patient (that is mean) was 5679.38 rupees which was significantly lower than the expected cost to be spent on transfusion as per CCTs (10562.89 rupees $p<0.001$). However considering the cost of investigations ,that is net cost spent per patient as per TEG was similar to as predicted by CCTs usage.

Figure 14: Comparison of cost spent on transfusion of blood products as per TEG in relation to CCTs

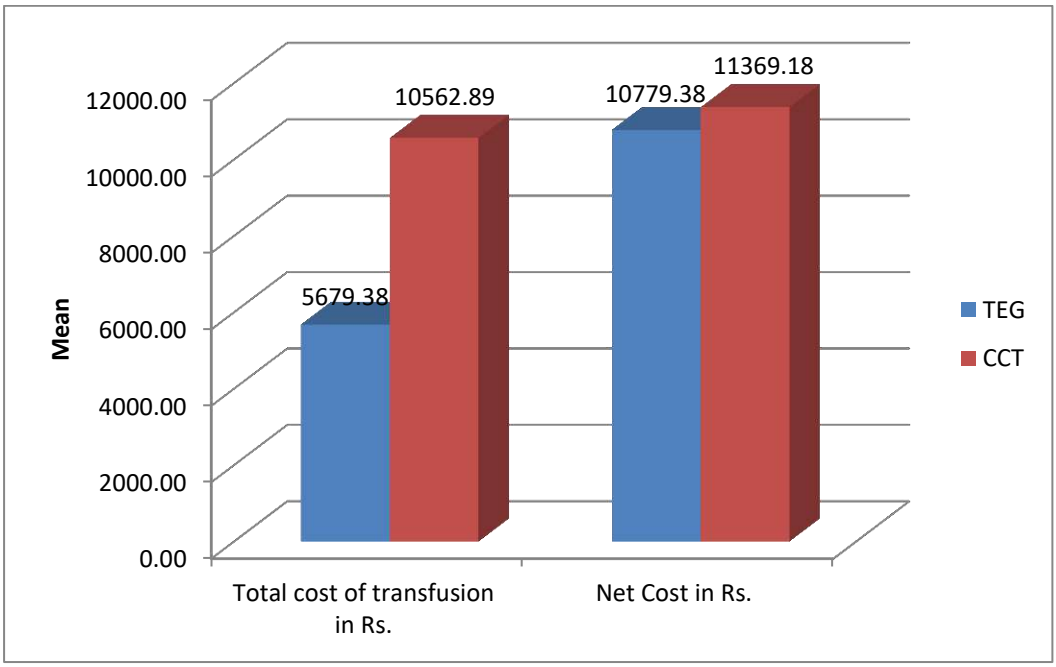


Table 16: Comparison of cost spent on transfusion of blood products as per TEG in relation to CCTs among patients who underwent low risk procedures

LOW	TEG		CCT		Z	p-value
	Mean	SD	Mean	SD		
Total cost of transfusion in Rs.	6554.84	6398.51	12517.74	5952.06	6.511	0.001
Net Cost in Rs.	11654.84	6398.51	12848.23	5951.33	1.303	0.197

Observation: Among patients who underwent low risk procedures (n=62), the total money spent on transfusion per patient (that is mean) was 6554.84 rupees which was significantly lower than the expected cost to be spent on transfusion as per CCTs (12517.74 rupees p<0.001). However considering the cost of investigations, that is net cost spent per patient as per TEG was similar to as predicted by CCTs usage.

Figure 15: Comparison of cost spent on transfusion of blood products as per TEG in relation to CCTs among patients who underwent low risk procedures.

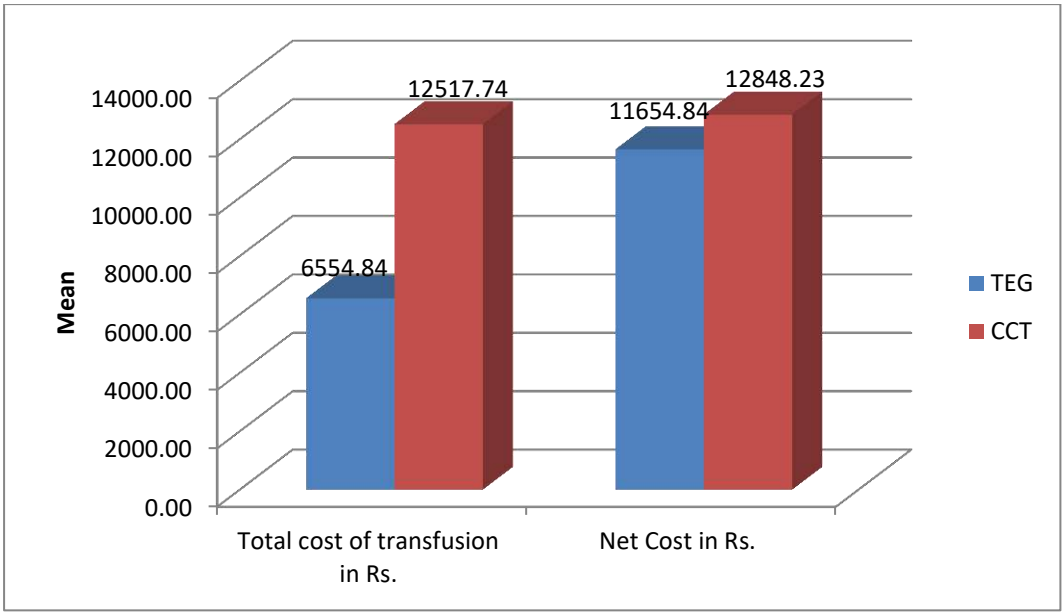


Table 17: Comparison of cost spent on transfusion of blood products as per TEG in relation to CCTs among patients who underwent high risk procedures.

HIGH	TEG		CCT		Z	p-value
	Mean	SD	Mean	SD		
Total cost of transfusion in Rs.	4128.57	6236.92	7100.00	5040.19	2.272	0.030
Net Cost in Rs.	9228.57	6236.92	8749.14	8947.73	-0.297	0.768

Observation: Among patients who underwent high risk procedures (n=35), the total money spent on transfusion per patient (that is mean) was 4128.57 rupees which was significantly lower than the expected cost to be spent on transfusion as per CCTs (7100.00 rupees p <0.030). However considering the cost of investigations, that is net cost spent per patient as per TEG was similar to as predicted by CCTs usage.

Figure 16: Comparison of cost spent on transfusion of blood products as per TEG in relation to CCTs among patients who underwent high risk procedures.

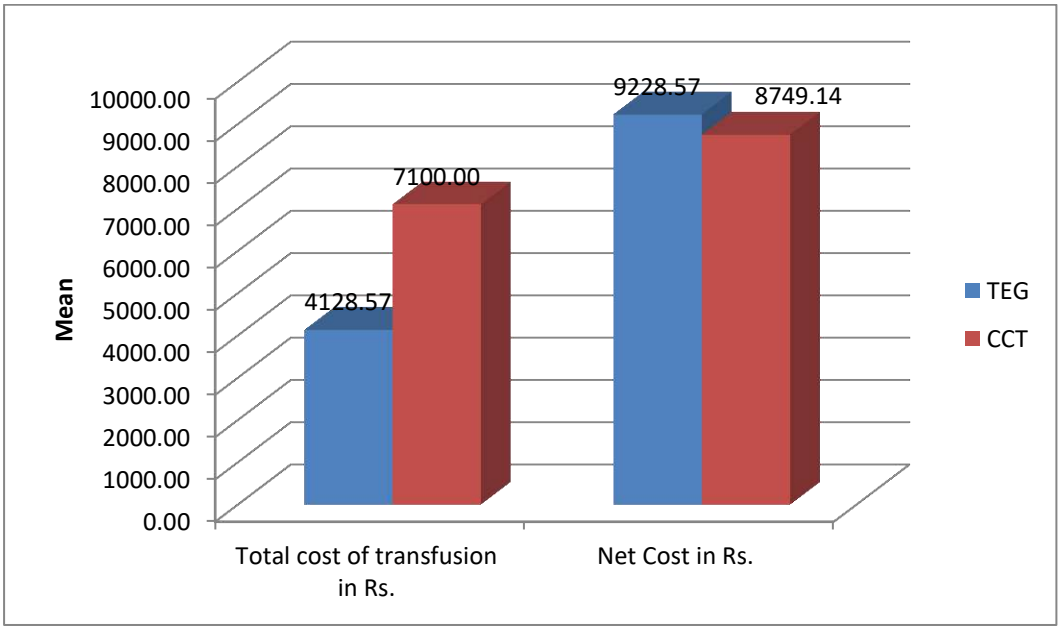


Table 18: Comparison of number of patients transfused FFP as per TEG in relation to CCTs overall

FFP		RISK OF BLEEDING				Total	Chi-square value	p-value
		Low		High				
TEG	no	62	100.0%	34	97.1%	96	0.177	0.184
	yes	0	0.0%	1	2.9%	1		
CCT	no	3	4.8%	1	2.9%	4	0.219	0.639
	yes	59	95.2%	34	97.1%	93		
p-value		0.001		0.001				

Observation: Among patients who underwent procedure with low risk of bleeding (n=62), 0.0% required FFP before procedure v/s 95.2 %would have needed FFP as per CCT (p value <0.001).Similarly, among patients who underwent procedure with high risk of bleeding (n=35) 2.9% required FFP before procedure v/s 97.1%would have needed FFP as per CCT.(p value<0.001)

Figure 17: Comparison of number of patients transfused FFP as per TEG in relation to CCTs overall

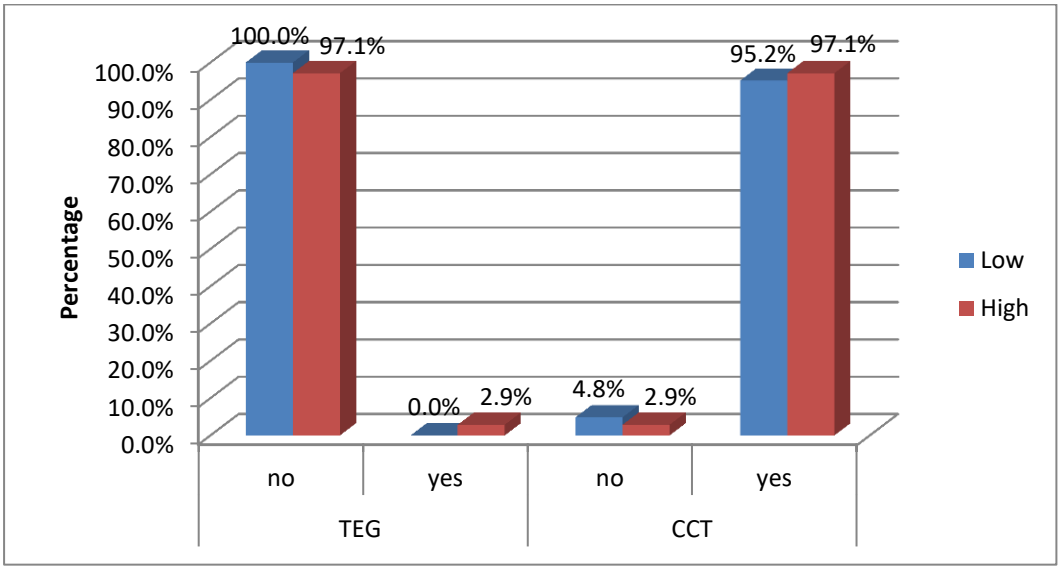


Table 19: Comparison of number of patients transfused platelet unit as per TEG in relation to CCTs overall

	PLTs Infused, Units	RISK OF BLEEDING				Total	Chi-square value	p-value
		Low		High				
TEG	no	30	48.4%	24	68.6%	54	3.655	0.056
	yes	32	51.6%	11	31.4%	43		
CCT	no	23	37.1%	28	80.0%	51	16.515	0.001
	yes	39	62.9%	7	20.0%	46		
p-value		0.206		0.278				

Observation: Among patients who underwent procedure with low risk of bleeding (n=62), 51.6% required platelet units before procedure v/s 62.9% would have needed platelet as per CCT.

Similarly ,among patients who underwent procedure with high risk of bleeding (n=35) 31.4% required platelet units before procedure v/s 20% would have needed platelet as per CCT indicating a functional defect in platelet not indicated by CCT (platelet count).

Figure 18: Comparison of number of patients transfused platelet unit as per TEG in relation to CCTs overall

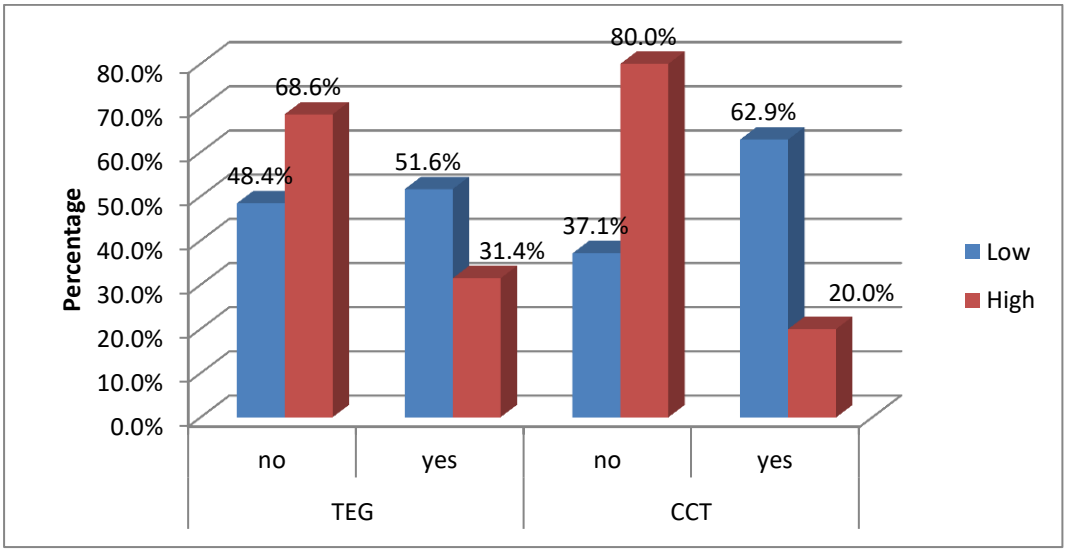


Table 20: Comparison of utilization of FFP among Child Pugh Classes as per TEG in relation to CCT

	FFP	TEG	TEG	CCT	CCT	Total	Chi-square value	p-value
CHILD PUGH CLASS	A	0	0.0%	3	75.0%	4	0.223	0.894
	B	0	0.0%	14	93.3%	15		
	C	1	1.3%	76	97.4%	78		
Total		1	1.0%	93	95.9%	97		

Observation: In 4 patients belonging to CPC A FFP were required in n= 3 patients as per CCT but were transfused in none as per TEG.

In 15 patients belonging to CPC B FFP were required in n=14 patients as per CCT but were transfused in none as per TEG.

In 78 patients belonging to CPC C FFP were required in n= 76 patients as per CCT but were transfused in n=1 as per TEG.

Figure 19: Comparison of utilization of FFP among Child Pugh Classes as per TEG in relation to CCT

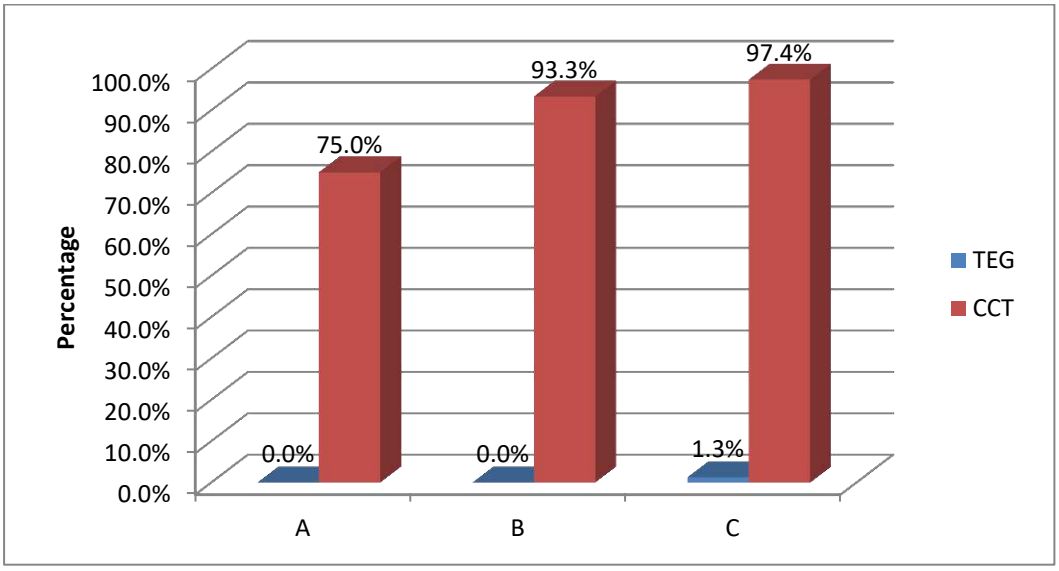


Table 21: Comparison of utilization of platelet units among various Child Pugh Classes as per TEG in relation to CCTs

	PLTs	TEG	TEG	CCT	CCT	Total	Chi-square value	p-value
CHILD PUGH CLASS	A	1	25.0%	4	100.0%	4	1.792	0.408
	B	6	40.0%	7	46.7%	15		
	C	36	46.2%	35	44.9%	78		
Total		43	44.3%	46	47.4%	97		

Observation: In 4 patients belonging to CPC A Platelet units were required in n=4 patients as per CCT but were transfused in n=1 as per TEG.

In 15 patients belonging to CPC B Platelet units were required in n=7 patients as per CCT but were transfused in n=6 as per TEG.

In 78 patients belonging to CPC C Platelet units were required in n= 35 patients as per CCT but were transfused in n=36 as per TEG.

Figure 20: Comparison of utilization of platelet units among various Child Pugh Classes as per TEG in relation to CCTs

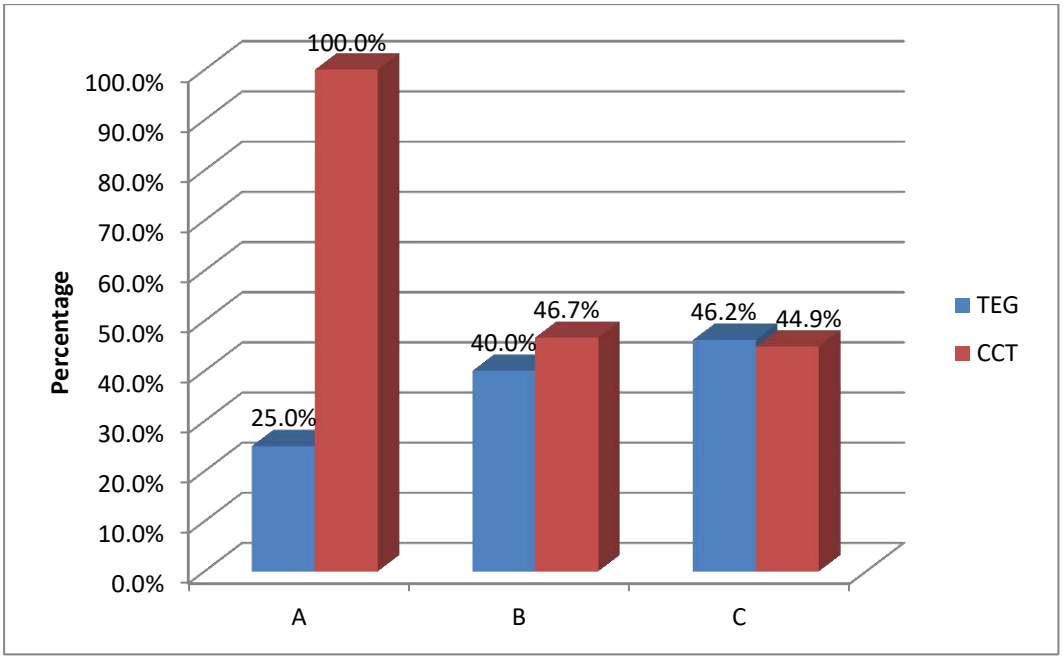


Table 22: Bleeding events in patients transfused as per TEG

TEG Bleeding event(ml)	No. of cases	Percentage
No	91	93.8%
< 200 ML	4	4.1%
> 200 ML	2	2.1%

Observation: Bleeding event post procedure in patients transfused as per TEG were observed in 6 patients only out of which significant blood loss >200ml was noted in 2 patients. However clinically significant bleeding requiring blood transfusion was observed in only one patient

Figure 21: Bleeding events in patients transfused as per TEG

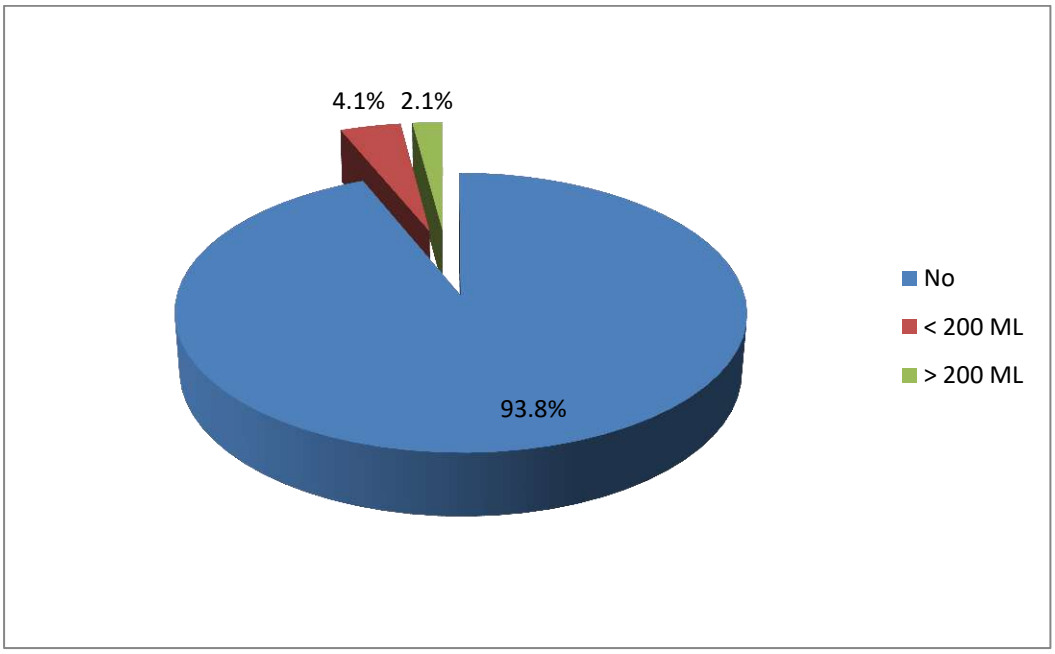


Table 23: Comparison of pre procedure and post procedure hemoglobin (gm/dl)

	PRE PROCEDURE		POST PROCEDURE		Z	p-value	Mean difference	Std. Deviation difference
	Mean	SD	Mean	SD				
HEMOGLOBIN (gm/dl)	9.70	1.45	9.64	1.45	2.798	0.006	0.06	0.21

Observation: The mean pre procedure hemoglobin was 9.70 gm/dl and mean post procedure hemoglobin was 9.64gm/dl .Only one patient who underwent incision and drainage for wound at leg had clinically significant bleeding and post procedure hemoglobin below 8g/dl and was hence transfused one packed cell post procedure.

Figure 22: Comparison of pre procedure and post procedure hemoglobin (gm/dl)

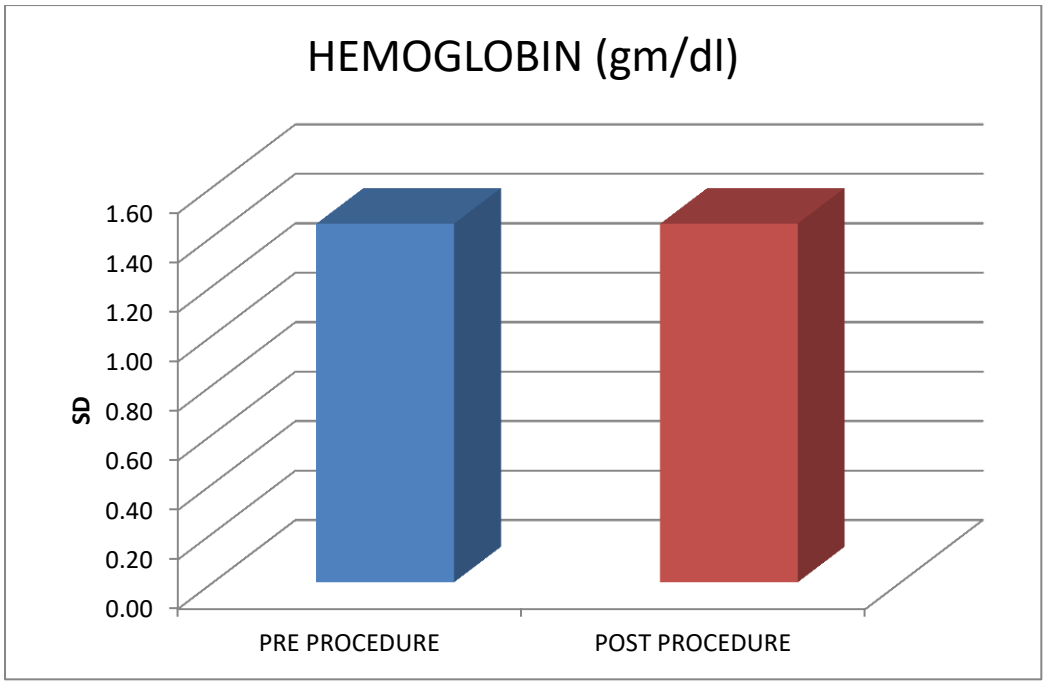


Table 24: Analysis of patients with bleeding event.

SR. NO	PROCEDURE	RISK OF BLEEDING	PLATELET COUNT (10^3/µl)	PT/INR	R VALUE (mins)	ALPHA ANGLE (degree)	MAX AMPLTIUDE (mm)	TRANSFUSION GIVEN (before procedure)	BLOOD LOSS (ml)
1	Hernia repair	High	40	17.3/1.33	2.1	56.1	42.2	-	100ml
2	Fasciotomy	High	120	18.2/1.66	6.5	53.7	43.7	-	200ml
3	Incision &Drainage	High	50	23.5.2.14	8.6	42.2	30.8	1SDP	1000ml
4	CVC insertion	Low	20	23.6/2.15	6.5	61.5	59.8	-	50ml
5	ERCP	High	50	20.8/1.90	5.4	62.8	32.4	1SDP	75ml
6	Debridement	High	92	7.1.55	2.2	70.8	52.3		100ml

Observation: Clinically significant procedure related bleeding was observed in only one patient out of 97 (1.03%), who underwent high risk procedure of incision and drainage for wound at leg. The investigations of patient were as follow platelet -50x 10^3/µl, PTI/INR(23.5/2.14) TEG result :R time (8.6 mins),K time (43.2 degree), MA (30.8 mm).Patient was transfused 1SDP units before surgery as per TEG . During surgery patient had 1000ml blood loss and was transfused 2FFP and 1 packed cell post surgery. No blood product transfusion reaction seen. Patient was followed upto 5 days daily post operation and no complication was observed.

DISCUSSION

Thromboelastography (TEG) and conventional coagulation tests (CCTs) like prothrombin time (PT), international normalized ratio (INR), and platelet count are crucial for assessing hemostasis, but they differ significantly in their approaches and the insights they provide. CCTs have been the traditional standard for evaluating coagulation abnormalities. PT/INR measures the extrinsic pathway and overall clotting ability, while platelet counts indicate the number of primary clotting cells. These tests are useful for predicting bleeding risks but are limited as they assess isolated parts of the coagulation process in vitro, not reflecting the complex in vivo environment, especially in patients with chronic liver disease (CLD), who often have a rebalanced coagulation state with simultaneous risks of bleeding and thrombosis.

The hemostatic state in cirrhosis is fragile, dynamic and can fluctuate between pro and anti-coagulant state depending on the concomitant risk factors. It is a common clinical practice to transfuse platelet units and fresh frozen plasma (FFP) in setting of gastrointestinal and non-gastrointestinal bleeding in patients with cirrhosis.

The British Society of Gastroenterology , British Society of Hematology and National Institute for Health and Care and Excellence recommend transfusion of FFP at PT/INR >1.5 and platelet unit at platelet count <50x10^3/µl before invasive procedures.[79-82] However, the American Association for the Study of Liver Diseases (AASLD) practice guidelines do not recommend correction of abnormal PT/INR with use of FFP.[87] We specially designed this study keeping in mind the dilemma in the guidelines regarding correction of coagulopathy. We used TEG in our study which was found to be better than CCT in terms of depiction of haemostasis, especially in cirrhosis as per various studies.

TEG being a whole-blood assay offers a more integrated view of hemostasis, capturing the functional interactions among all coagulation components including platelets, fibrinogen, and clotting factors .This holistic view allows clinicians to assess not just the presence of

coagulation defects but their functional impact on hemostasis. The practical advantages of TEG are significant. It delivers rapid, point-of-care results essential for acute settings like trauma, cardiac surgery, and liver transplantation, allowing for immediate and targeted intervention.

The aim of the study was to define the role of TEG in defining the blood product transfusion in patients with cirrhosis before an invasive procedure. In this prospective observation study, patients were evaluated from 15th September 2022 to 31st December 2022 and 1st July 2023 to 31st December 2023 in department of General Medicine, Gastroenterology, Cardiology, Surgery and Intervention Radiology at Dayanand Medical College and Hospital, Ludhiana.

All consenting adults with cirrhosis and coagulopathy, defined as PT/INR >1.5 and a platelet count <50x10^3/µl, planned for an invasive procedure were included .Total 350 patients were screened out of which 97 underwent TEG and TEG guided blood products (FFP/ platelet unit transfusion)before the invasive procedure which was compared to predicted transfusion as per CCT guidelines. Hence the confounding role of various factors aetiology, age, gender, child Pugh class was eliminated and this provide internal validity to our results.

For real life scenarios our study included all Child Pugh class .The most common cause of cirrhosis in our study was alcoholic liver disease (80.4%) followed by metabolic associated steatotic liver disease. Majority of patients were male (92.8%) and belonged to Child Pugh class C.This could be attributed to the regional variation in aetiology of CLD.

The TEG group received FFP if Reaction time (R) >14 mins and platelet units for Maximum amplitude (MA) ≤ 40mm.[75] The predicted requirement as per CCT was calculated using the indication: FFP given if PT/INR >1.5 and platelet units for platelet count <50x10^3/µl.[78-82] The risk of bleeding associated with a procedure was classified as high risk (as those associated with bleeding risk >3%) and low risk (as those with bleeding risk <3%).[38] The procedures with low risk of bleeding were central venous catheter insertion (38.1%), dialysis

catheter insertion (12.4%), ascitic tap (12.4%)and pleural tap (1%).The procedures with high risk of bleeding were endoscopic variceal ligation (14.4%) ,percutaneous drainage insertion (7.2%),liver biopsy , biopsy from other site(mesenteric lymph node), debridement of cellulitis, hernia repair , incision & drainage and fasciotomy.

In our study, all patients required blood product transfusion as per CCT whereas only 43 were actually transfused as per TEG (100% v/s 44% p= 0.001).As per CCT only FFP were required in 51 out of 97 patients (52.6%),only platelet units in 4 patients(4.1%) and both FFP and platelet in 42 patients (43.3%).In our study using TEG based transfusion only one patient was transfused both FFP and platelet (1% v/s 43.3% in CCT group), only FFP in none (0%v/s 52.6% in CCT group) and only platelets were transfused in 42 patients (43.3% v/s 4.1% in CCT group).However it was worth noting that among patients undergoing high risk procedures only one patient required FFP (along with platelets)as per TEG. Requirement of platelet unit was lower in low risk procedure group as per TEG when compared to predicted requirement as per CCT ,but this difference was not statistically significant .The mean amount of FFP transfused was 10.31 ml as per TEG which was statistically significant and lower than predicted transfusion of 945.88 ml as per CCT. However, not much difference seen in platelet units requirement. Our study indicated a significant reduction in total cost of transfusion as per TEG (mean cost of transfusion 5679.38 rupees v/s 10562.89 rupees in CCT p =0.001).But the net cost (including the cost of investigation) hardly varied. The lack of well acceptability and clear data regarding the role of TEG and guidelines make TEG a costly investigation which acts as hindrance in its use role in defining hemostasis in cirrhosis.

As per our study, clinically significant procedure related bleeding was observed in only one patient out of 97 (1.03%), who underwent high risk procedure of incision and drainage for wound at leg. The investigations of patient were as follow platelet count -50 x 10^3/µl , PT/INR(23.5/2.14)and TEG result were :R time (8.6 mins),K time (42.2 degree), MA (30.8 mm).Patient was transfused 1SDP (single

donor platelet) unit before surgery as per TEG . During surgery patient had 1000ml blood loss and was transfused 2FFP and 1 packed cell post surgery. No blood product transfusion reaction seen. Patient was followed upto 5 days daily post operation and no complication was observed. This bleeding event could be procedure related local complication or can be due to requirement of cryoprecipitates which were not given by treating team (as the K value indicates fibrinogen deficiency as well as platelet function). No clinically significant bleeding was seen in any patient who underwent low risk procedure (transfused according to TEG). Our results hence highlight the reliability of TEG to safely guide blood product transfusion therapies before invasive procedures in patients with cirrhosis without increase in risk of bleeding or transfusion related reactions.

The rebalanced hemostasis in cirrhosis could be the explanation to the low observed bleeding rate in this study. This emphasizes the futility of overzealous blood product transfusion based on conventional tests.

Even though all patients selected for study had coagulopathy as per CCT and hence had an indication for transfusion as per CCT. However the reduced requirement as per TEG and occurrence of clinically significant bleeding in only one patient indicated a need for a better approach to monitor hemostatsis in cirrhosis. Previous studies have demonstrated that variceal rebleeding rates are typically higher among patients who receive liberal transfusions compared to those receiving restricted transfusions of blood products. Elevated portal pressure following volume transfusions can contribute to an increased risk of rebleeding. Additional concerns associated with blood products include transfusion reactions, circulatory overload, and the potential transmission of infections.

Our results validated the American Gastroenterological Association (AGA) guidelines that PT/INR is not recommended for FFP transfusion.[66]

Liver cirrhosis is now considered as a prothrombotic rather than naturally hemorrhagic state. Most clinicians facing patients with coagulopathy transfuse the patients with fresh frozen plasma (FFP)

and/or platelets, fearing that the impaired clotting will translate in a higher risk of bleeding. Review of literature has shown very few prospective trials for bleeding in routine procedures in cirrhotic patients with coagulopathy. In particular, there is little evidence for the effectiveness of the prophylactic use of FFP. There are no clear guidelines for cut off values of CCTs beyond which invasive procedures should be avoided. There is an on going debate regarding the role of platelet count and PT/INR as forecaster of risk of bleeding in patients with cirrhosis.

In 2007 results from a study done by **Tripod et al.** showed that in cirrhosis, PT/INR did not predict the bleeding risk and it provides a robust measure of liver function and predicts the mortality of acute and chronic liver disease.[88]

The study conducted by **Napolitano et al.** showed that post-procedural bleeding is uncommon in cirrhotic patients with abnormal PT/INR or low platelet counts who underwent invasive procedures.[89] Moreover, the study found that these abnormal lab values did not reliably predict the risk of bleeding after such procedures.

An Indian study by **Shah et al.** also concluded that conventional coagulation parameters were not reliable predictors of clinically significant bleeding in cirrhosis patients.[90] Other studies observed that prophylactic platelet transfusions only slightly improved platelet count and thrombin generation, and thromboelastography (TEG) parameters did not necessarily normalize.

A 2020 study by **Vuyyuru et al.** demonstrated that, despite pre-procedural platelet transfusions, platelet counts remained below 50,000/mm³ in the control group.[91] However, no procedure-related bleeding was observed, suggesting that achieving a platelet count higher than 50,000/mm³ may not be necessary to prevent bleeding complications. A recently published guideline by **Nadim et al.** also recommends against routine prophylactic use of fresh frozen plasma.[92]

In our study patients with platelet count < $50x10^3$/µl were 44(45.4%) and platelet count <$30x\ 10^3$/µl were 19(19.5%). 91 patients (93.8%)

had PT/INR >1.5 , 44(45.4%) had PT/INR >2.5 and 33(34%) had PT/INR >3.No transfusion of blood products in cirrhotic patient with coagulopathy before an invasive procedure is risky and a preventable cause of complications to the patient.

In a study in 2018 by **Jing Li et al.** including 874 cirrhotic patients who underwent invasive procedures ,296 patients (33.9%) had coagulopathy.[74] Major bleeding following invasive procedures occurred in 21 patients (2.4%) and was more prevalent in those with coagulopathy compared to those without (4.1% vs 1.6%, P = 0.023). Major bleeding was also more common in patients with severe thrombocytopenia (platelet count <50 $x10^3$/μL) than in those without (4.9% vs 1.6%, p = 0.008). There was no significant difference in the incidence of major bleeding between patients with an INR ≥ 1.5 and those with an INR < 1.5 (4.5% vs 2.0%, p = 0.065). However, patients with an INR ≥ 1.5 had a significantly higher in-hospital mortality rate compared to those with an INR < 1.5 (6.4% vs 1.3%, p < 0.001). The study concluded that severe thrombocytopenia was associated with increased risk of major bleeding after invasive procedures in cirrhosis, and an INR ≥ 1.5 is associated with an increased in-hospital mortality.

Similarly, **Cocero et al**. (2016) found that patients with chronic liver disease who had a platelet count >40 × 10^3/μL and an PT/INR of <2.5 had a relatively low risk of bleeding, but an PT/INR of ≥2.5 and platelet count ≤40×10^3/μL represented significant risk factors of bleeding after dental extractions.[93]

Giannini et al. also determined that the bleeding risk after invasive procedures was connected to the extent of thrombocytopenia in patients with advanced liver diseases, but it was not related to PT/INR levels.[11]

The risk of bleeding during liver biopsy varies significantly based on patient's platelet counts and PT/INR levels, as highlighted by recent studies. **Takyar et al.** reported an overall bleeding rate of 0.6% in 3,357 biopsies, but this risk increased to 4.8% among patients with platelet counts below 60 $x10^3$/μL.[94]

Similarly, findings from the HALT-C (Hepatitis C Antiviral Long Term Treatment against Cirrhosis) trial showed that while patients with platelet counts over 150 $x10^3$/µl had a low bleeding risk of 0.2%, those with counts ≤60 $x10^3$/µL faced a substantially higher risk of 5.3%. Additionally, patients with an INR ≤1.1 had a bleeding rate of 0.4%, whereas those with an INR ≥1.3 experienced a higher rate of 2.4%. These studies emphasize the importance of assessing coagulation state prior to liver biopsy to minimize the risk of bleeding complications.[95]

In 2009 **Tripodi et al.** showed that thromboelastometry is suitable for investigating bleeding risk in stable cirrhosis.[96]

In 2010 study conducted by **Wang et al.** involving 28 patients undergoing orthotopic liver transplantation who were randomly assigned to two groups.[97] One group was monitored using point-of-care TEG analysis during surgery, while the other group was monitored using conventional laboratory measures of blood coagulation. Patients in the control group received transfusions of blood products (platelets, PT/INR, fibrinogen) when their levels fell below specified thresholds: platelets <50 $x10^3$/µL, PT/INR >1.5, and fibrinogen <1g/L. In contrast, the TEG-monitored group received transfusions based on TEG parameters: R-time >10 mins, MA <55 mm, and alpha angle <45 degrees. The study found that patients monitored with TEG required significantly less fresh frozen plasma (FFP) on average (12.8 ± 7.0 units) compared to those monitored with standard laboratory measures (21.5 ± 12.7 units). Although there was a trend towards reduced blood loss in the TEG-monitored patients, this difference was not statistically significant. The study also noted no significant differences in total fluid administration or three-year survival rates between the two groups. Unfortunately, this study was not powered to evaluate patient-centered outcomes (e.g. adverse events from blood transfusion).

In 2016, **De Pietri et al.** conducted a study focusing on blood product transfusion practices in patients with cirrhosis who had significant coagulopathy, defined as an INR >1.8 and/or platelet count <50 x 10^3/µL, and were scheduled for invasive procedures. Sixty patients

were randomly divided into either a TEG-guided transfusion strategy or standard of care (that is CCTs based)(SOC group) in a 1:1 ratio. According to the study protocol, all patients in the SOC group received blood product transfusions, whereas only 5 patients in the TEG group received transfusions (16.7% vs. 100%, respectively; $p < 0.0001$). Specifically, none of the TEG-guided patients received fresh frozen plasma (FFP) alone ($p < 0.0001$ compared to SOC), 2 received platelets (6.7%, $p = 0.009$ compared to SOC), and 3 received both FFP and platelets (not statistically significant).This study highlighted that TEG-guided transfusion strategies significantly reduced the overall need for blood product transfusions compared to standard practice in patients with cirrhosis undergoing invasive procedures.[38]

The key finding of the study was that only one patient in the entire cohort (2%) experienced post-procedure bleeding. This patient underwent a large-volume paracentesis, which is considered a low-risk procedure for bleeding, and had received fresh frozen plasma (FFP) before the procedure. This suggests that the risk of post-procedure bleeding was not directly related to the presence or correction of coagulopathy, but rather to potential local complications of the procedure itself, such as damage to blood vessels in the abdominal wall during paracentesis.

Additionally, the study observed that both in the TEG-guided and standard care (SOC) groups, blood product transfusions occurred more frequently in low-risk procedures rather than high-risk ones. Despite this, the incidence of procedure-related bleeding did not increase significantly. In summary, the study indicates that while blood product transfusions were administered more often in low-risk procedures by chance, the risk of procedure-related bleeding did not show a significant increase, emphasizing the importance of procedural factors in determining bleeding risk rather than solely focusing on coagulopathy or its correction.

However, the following issues should be noted that the number of patients included was relatively small ($n = 60$) and all included patients were diagnosed with coagulopathy hence no control group without

coagulopathy was established. Also only one patient developed major bleeding after an invasive procedure which carried a low risk of bleeding, and therefore, the statistical power of the study is questionable.

In a prospective study conducted by **Somani et al.** in 2016 involving 150 cirrhotic patients undergoing invasive procedures, comprehensive coagulation tests (CCTs) including bleeding time, clotting time, PT/INR, aPTT (activated partial thromboplastin time) and platelet count, as well as thromboplastin generation time (TGT) and thromboelastography (TEG), were employed to assess bleeding risk.[98] Interestingly, bleeding time, clotting time, and thromboplastin generation time were normal for all 150 patients, and only one patient experienced clinically significant post-procedural bleeding. The study did not find a significant statistical association between bleeding events and INR, aPTT, platelet count, or Child-Pugh class. Despite the presence of abnormal CCT results in many patients, a significant proportion showed normal TEG measurements, specifically R time (61%) and MA value (75%). These findings suggest that abnormal traditional coagulation tests in cirrhotic patients may not reliably predict bleeding risk, highlighting the potential usefulness of TEG in evaluating bleeding risk in this population.

In a randomized controlled trial by **Kumar et al.** (2020), 96 patients with cirrhosis experiencing active nonvariceal bleeding were divided into two groups: a thromboelastography (TEG)-guided transfusion strategy group and a standard-of-care coagulation-based transfusion (that is CCT based/SOC) group[65]. The TEG-guided transfusion criteria included R time >10 mins, MA <55 mm, and alpha angle K <45 degrees. In the TEG group, significantly fewer patients (26.5%) received transfusions of all three blood components (fresh frozen plasma [FFP], platelets [PLTs], and cryoprecipitate) compared to the CCT group (87.2%, $p < 0.001$). Moreover, 7 patients (14.3%) in the TEG group received no blood component transfusions, whereas none in the CCT group received no transfusion ($p = 0.012$).

The study found no significant differences between the groups in their ability to control bleeding, failure to prevent rebleeding, or mortality

rates. However, serious transfusion-related reactions were significantly less common in the TEG group, with 15 patients (30.6%) experiencing any transfusion-related reaction compared to 35 patients (74.5%) in the SOC group ($p < 0.001$). Overall, the trial highlighted that a TEG-guided transfusion strategy in patients with cirrhosis and active nonvariceal bleeding resulted in more targeted use of blood components and a lower incidence of serious transfusion-related reactions compared to standard coagulation-based transfusion practices. However in this study patients with PT/INR >1.8 were 90% of patients in control group v/s patients with R-time >10 minutes were 60% of patients in TEG group. Similarly patients with platelets count <50x 10^3µ/l were 80% of patients in control v/s patients with MA < 55mm were 53% of TEG group. Fibrinogen function was<80 mg/dL in 90% patients of control v/s Alpha-angle <45 degrees was in 60% of patients in TEG group. It is obvious from these baseline characteristics that patients in the TEG arm will receive fewer blood products. And this was indeed demonstrated by the results patients in the TEG arm received fewer of every type of blood product. In addition, the primary outcome chosen was the amount of FFP transfused, rather than a clinical-based bleeding outcome.

In 2020, **Rout et al.** conducted a study evaluating thromboelastography (TEG)-directed blood product transfusion in patients with cirrhosis experiencing acute variceal bleeding.[99] In the TEG group, patients received fresh frozen plasma (FFP) if their R value was >15 minutes and MA was <30 mm. Notably, the study used native TEG rather than kaolin-activated TEG, which is typically faster and more commonly used in guiding transfusions during hemorrhage.The study included 60 patients, with 30 randomized to each group (TEG-guided and conventional transfusion). Four patients in the TEG group received blood product transfusions compared to all patients in the conventional transfusion group (13.3% vs. 100%; $p < 0.001$). Initial control of bleeding during endoscopy and rebleeding rates at 5 days were similar between the two groups. However, rebleeding events at 42 days were fewer in the TEG group. This study suggests that TEG-

guided transfusion strategies may result in reduced overall blood product transfusions compared to conventional methods in patients with cirrhosis and acute variceal bleeding, while maintaining similar short-term control of bleeding and potentially reducing rebleeding rates over the longer term. However the study did not measure fibrinogen level and none of the patients were transfused with cryoprecipitate. The TEG parameters after blood transfusion were not reassessed. The lack of a control arm that did not receive any prophylactic products. Similarly, this study did not establish a clinically-based primary outcome and focused on evaluating the volume of fresh frozen plasma (FFP) transfused. Additionally, variceal bleeding, a complication of portal hypertension, is primarily caused by elevated portal pressure rather than hemostatic failure. Therefore, the practice of prophylactic transfusion is contentious in this context, regardless of whether TEG or INR parameters are used, and could potentially exacerbate portal hypertension.

In a study in 2020 by **Vuyyuru et al.** 341 patients with cirrhosis were screened, out of which 58 were selected for high risk procedures and randomized into TEG and CCT.[91]The TEG group received blood products FFP if R time >14 min and platelet units if MA <32mm.This study used Mono TEM A device. The most frequently performed procedure was a percutaneous plug liver biopsy (82.7%). In the TEG group, only nine patients required transfusions compared to all patients in the CCT group (31% vs. 100%; p =0.001). Additionally, only two patients (6.9%) in the TEG group received platelet transfusions, while 72.4% (n=21) in the CCT group did. No patients in either group experienced bleeding-related complications or required blood transfusions within the first five days post-procedure. There were no instances of fluid overload or transfusion reactions, and no significant differences in pre- and post-procedure hemoglobin levels were observed in either group.However the study had some limitations as it included only high risk procedure. The amount of FFP transfused was lesser than recommended (5 ml/kg), fibrinogen was not considered and no post transfusion TEG results analysis was done.

Stravitz et al. investigated hemostasis in patients with acute liver failure (ALF) using thromboelastography (TEG). Despite presenting with markedly elevated INR levels, these patients exhibited normal hemostasis as indicated by TEG results. These findings provide valuable insight into the discrepancy observed by clinicians managing patients with ALF, where traditional coagulation tests show severe abnormalities but there is no apparent clinical evidence of hemostatic failure, such as spontaneous bleeding.[100]

All the studies demonstrate a decreased utilization of blood products in patients with cirrhosis and coagulopathy.

De Pietri et al.demonstrated decreased utilization of FFP with not much difference of platelet in cirrhotic before an invasive procedure. In contrast **Vuyyuru et al.** found a significant decreased in need of platelet rather than FFP. **Kumar et al.** and **Rout et al.** showed decreased utilization of both FFP and platelet.

The five studies above can be split between two TEG-based strategies. **Wang et al.** & **Kumar et al.** associated with transfusion of cryoprecipitate whereas **Rout et al., De Pietri et al.** and **Vuyyuru et al.** did not consider cryoprecipitate transfusion.

The indication of transfusion as per TEG guidelines varied among the studies. Fibrinogen is not done commonly as part of CCTs. The patients with cirrhosis (irrespective of PT/INR, platelet count) who bleed might be due to requirement of cryoprecipitate which are not routinely considered.

TEG acts as single investigation to provide overall requirement of all blood products.

We also need studies comparing the influence of different laboratory cut off points (both by using TEG parameters and standard coagulation tests) on the amount of blood component transfused.

Our study showed significant decrease in need of FFP in patients with cirrhosis with coagulopathy undergoing invasive procedure .However the platelet utilization did not vary significantly and may be a result of high cut off of MA value.

Limitations

We aimed to improve the MA parameter in TEG through platelet transfusions. However, we did not assess fibrinogen levels before the procedure, which also affects MA. As fibrinogen is not a part of routine CCTs in our hospital. We did not analyse the requirement of cryoprecipitate in our present study. Although if indicated as per TEG results patients were given cryoprecipitate, if the treating team agreed. Additionally, we did not track changes in TEG parameters after administering blood products, which could have helped establish optimal targets for correcting these parameters. A majority of our study participants were classified as Child C status, and most procedures were scheduled electively. We did not account for sepsis, a significant factor contributing to coagulation abnormalities in cirrhosis. We also lacked a control group that did not receive prophylactic products, which could have provided a comparative baseline. The cost of TEG testing was a limiting factor, which may have affected our ability to observe a significant difference in overall cost reduction between the TEG and conventional coagulation testing (CCT) groups.

SUMMARY AND CONCLUSION

Patients with cirrhosis have a rebalanced state of hemostasis. They can be hypercoagulable/hypercoagulable states. Recent guidelines state that platelet count and PT/INR do not predict the risk of bleeding as they provide a tip-of-the-iceberg picture of hemostasis and deranged results of CCT should not be used as an indication for transfusion of blood products in such patients before an invasive procedure. The risk of bleeding overall in patients with cirrhosis is unpredictable and cannot be stated to be dependent on one factor. However, before an invasive procedure, the risk of bleeding in patients with significantly elevated PT/INR and or severe thrombocytopenia cannot be ignored. It is a preventable complication. Our study aimed to define the role of TEG as a better investigation to form a basis for transfusion in patients with cirrhosis undergoing invasive procedures.

In summary, for patients with cirrhosis and coagulopathy undergoing invasive procedures, adopting a pre-procedure TEG-guided transfusion approach results in notably reduced blood product usage compared to conventional coagulation-based transfusion strategies relying on INR and platelet count, all without an associated increase in bleeding risk.

Table 25: Overall conclusion of results

	TEG GROUP	CCT GROUP	P value
FFP or platelet transfused (n)	43	97	0.001
FFP (n) Low risk procedure High risk procedure	 0 1	 59 34	 0.001 0.001
Mean amount FFP infused (ml) Low risk procedure High risk procedure	10.31 0.00 28.57	943.88 943.55 950	0.001 0.001 0.001
Platelet only (n) Low risk procedure High risk procedure	 32 11	 39 7	 0.206 0.277
Total cost of transfusion(rupees)	5679.38	10562.89	0.001
Net cost (rupees)	10779.38	11369.18	0.241
Transfusion related side effect	none	Assumed to be none	
Clinically significant bleeding (n)	1	Assumed to be none	
RBC transfusion post procedure (n)	1	Assumed to be none	

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SR. NO.	MRD NO	INTIALS	AGE (Year)	GENDER	AGE GROUP	ADDRESS	CONTACT NO	BODY WEIGHT (Kg)	IDEAL BODY WEIGHT (Kg)	ETILOGY	ASCITES	HEPATIC ENCEPHALOPATHY	MELD SCORE	CHILD PUGH CLASS
1	1350891	ZS	59	M	3	Ludhiana	9876432186	60	-	Autoimmune Liver Disease	-	-	16	B
2	1364569	NS	61	M	4	Barnala	9878653857	65	-	Alcholic Liver Disease	grade 2	grade3	26	C
3	37571	M	53	M	3	Bathinda	9815438741	67	-	Alcholic Liver Disease	-	-	10	A
4	1359972	TS	61	M	4	Jalandhar	9888304115	79.8	77.6	Metabolic associated steatotic liver disease	grade 2	grade3	24	C
5	904278	S	42	M	2	Bathinda	9463404464	68	-	Alcholic Liver Disease	grade 2	grade3	24	C
6	1361585	MS	55	M	3	Mohali	9876524984	50	-	Alcholic Liver Disease	-	grade1	28	B
7	1067008	DS	49	M	2	Roop Nagar	9592226831	98	60	Metabolic associated steatotic liver disease	grade 3	grade1	25	B
8	1364573	AS	49	M	2	Muktsar	9782800044	71	-	Metabolic associated steatotic liver disease	-	-	9	A
9	1313028	SS	49	M	2	Bathinda	9882514152	85	77.6	Alcholic Liver Disease	grade 3	grade3	23	C
10	1221385	VS	52	M	3	Mohali	9876524411	105	-	Alcholic Liver Disease	-	-	22	B
11	1366841	KG	40	M	1	Amritsar	9419100071	90	68.4	Alcholic Liver Disease	grade 2	grade2	30	C
12	1375472	MK	35	M	1	Jalandhar	9876983333	90	-	Alcholic Liver Disease	-	-	12	C
13	1345507	PS	53	M	3	Ludhiana	9846724321	68	63.8	Alcholic Liver Disease	grade 2	-	12	C
14	1401163	RK	54	M	3	Jamu	9419247691	63	56.9	Alcholic Liver Disease	grade 2	grade3	28	C
15	1407588	LS	55	M	3	Jalandhar	977711826	68	-	Alcholic Liver Disease	grade 2	-	33	C
16	1286113	G	41	M	2	Ludhiana	9888191122	87.1	63.8	Alcholic Liver Disease	grade 3	grade3	27	C
17	944068	JS	43	M	2	Mansa	9876576489	73	63.8	Alcholic Liver Disease	grade 1	-	37	C
18	1411001	KK	55	M	3	J&K	9419741824	78.8	-	Alcholic Liver Disease	-	-	25	C
19	1384499	SS	38	M	1	Jalandhar	8462469812	50	59.2	Alcholic Liver Disease	-	grade3	20	C
20	27889	GS	65	M	4	Mansa	9855065263	70	68.4	Alcholic Liver Disease	grade 2	grade2	17	C
21	1300562	GS	54	M	3	Hoshiarpur	9872350748	70	66.6	Alcholic Liver Disease	grade 3	grade2	24	C
22	1402470	MS	32	M	1	Ludhiana	9914523840	110	73	Alcholic Liver Disease	grade 2	grade3	33	C
23	1338123	JS	55	M	3	Malerkotla	7589179171	69	61.5	Alcholic Liver Disease	grade 3	-	12	B
24	1379311	VK	35	M	1	Jalandhar	9877588164	68	59.2	Alcholic Liver Disease	grade 3	-	27	C
25	1313128	SS	49	M	2	Hoshiarpur	8264295984	80	63.8	Alcholic Liver Disease	grade 3	grade2	16	C
26	1385601	LK	45	F	2	Jalandhar	9501611036	54	-	Metabolic associated steatotic liver disease	grade 3	grade3	25	C
27	1383118	NS	56	M	3	Bathinda	9463553108	69	68.4	Alcholic Liver Disease	grade 2	grade2	30	C
28	1402058	LS	26	M	1	Moga	9855710388	65	-	Alcholic Liver Disease	-	grade3	37	C
29	1347055	SD	68	F	4	Bathinda	9463336066	50	-	Autoimmune Liver Disease	grade 1	grade3	22	C
30	1385975	RS	50	M	2	Bathinda	9653840945	65	-	Alcholic Liver Disease	grade 1	grade3	31	C
31	1300462	GS	58	M	3	Hoshiarpur	8872887488	80	77.6	Alcholic Liver Disease	grade 3	-	23	C
32	1135946	BS	32	M	1	Jalandhar	9988587013	50	-	Alcholic Liver Disease	grade 3	grade4	41	C
33	477218	VS	48	M	2	Ludhiana	9815677956	50	-	Alcholic Liver Disease	grade 1	grade3	41	C

SR. NO.	MRD NO	INTIALS	HCC	PROCEDURE	RISK OF BLEEDING	HEMOGLOBIN (gm/dl)	WBC (10^3/ul)	PLATELET COUNT (10^3 /Ul)	PTI	INR	TEG R VALUE (Mins)	TEG Alpha Angle (Degree)	TEG Max Amplitude (MM)	CCT Total amount of FFP Infused, mL	CCT Total amount of PLTs Infused, Units
1	1350891	ZS	N	Liver Biopsy	high	10	7	100	19.2	1.75	5.1	54.5	42.89	1000	0
2	1364569	NS	N	CVCInsertion	low	8.5	7.8	47	50.1	4.1	1.2	36.8	42.1	1000	1SDP
3	37571	M	N	Hernia Repair	high	11.2	3.12	40	17.3	1.33	2.1	56.1	42.2	1000	1SDP
4	1359972	TS	N	CVCInsertion	low	8.2	20.43	116	52.1	4.3	2.8	58.1	40.8	1250	0
5	904278	S	N	Ascitic Tap	low	8.9	5.8	60	50.4	4	5.1	54.7	35.2	1000	0
6	1361585	MS	N	DCInsertion	low	11.7	1.9	32	17.2	1.57	3.5	72.7	52.3	750	1SDP
7	1067008	DS	N	Ascitic Tap	low	9.7	5.4	38	16.3	1.49	3.2	47.5	29.8	0	1SDP
8	1364573	AS	N	PCNL Insertion	high	12.4	3.67	40	1.39	1.27	1.8	45.4	29.6	0	1SDP
9	1313028	SS	N	Ascitic Tap	low	11	5	48	51.1	4.3	7.5	38.8	32.5	1250	1SDP
10	1221385	VS	N	Fasciotomy	high	12	6	120	18.2	1.66	6.5	53.7	43.7	1500	0
11	1366841	KG	N	DCInsertion	low	12	6	251	35.7	3.24	7.2	67.5	42.5	1000	0
12	1375472	MK	N	DCInsertion	low	8	7	152	35.2	3.6	5	72.6	51.6	1250	0
13	1345507	PS	N	Incision & Drainage	high	8.5	10.3	50	23.5	2.14	8.6	42.2	30.8	1000	1SDP
14	1401163	RK	N	CVCInsertion	low	8.9	6.2	18	20.9	1.9	3.2	49.2	23.1	750	1SDP
15	1407588	LS	N	CVCInsertion	low	8.1	18.9	50	49.1	4	8.6	44	37.4	1000	1SDP
16	1286113	G	N	PCD Insertion (Pleural effusion)	high	8	6.8	200	21.6	1.97	3.6	56.8	52	1000	0
17	944068	JS	N	CVCInsertion	low	9.1	6.4	154	60	5.1	4.8	67.5	46.6	1000	0
18	1411001	KK	N	CVCInsertion	low	11.9	14.1	244	40	4.2	2.7	69.3	52.1	1250	0
19	1384499	SS	N	EVL	high	8.5	15	134	24.6	2.24	15.6	7.7	6.5	1000	0
20	27889	GS	N	CVCInsertion	low	12.2	7.8	47	35.3	3.2	6.5	54.3	35.5	1000	1SDP
21	1300562	GS	N	Liver Biopsy	high	9.8	4.8	126	30.7	2.79	5.2	33.3	23.3	1000	0
22	1402470	MS	N	CVCInsertion	low	10.2	8.3	24	27.3	2.48	5.8	62.5	34.2	1000	1SDP
23	1338123	JS	Y	Liver Biopsy	high	10.5	14.88	216	16.3	1.6	2.9	71.2	54.3	1000	0
24	1379311	VK	N	PCD Insertion (Pleural effusion)	high	9.8	19	171	22.9	2.09	0.4	47.9	23.6	1000	0
25	1313128	SS	N	Pleural Tap	low	7.9	21	142	23	2.09	7.5	38.8	32.5	1000	0
26	1385601	LK	N	CVCInsertion	low	10.6	8.9	26	26.1	2.37	12.3	49.2	43.3	750	1SDP
27	1383118	NS	N	CVCInsertion	low	8.9	15	46	23.8	2.17	3.2	52	46.6	1000	1SDP
28	1402058	LS	N	DCInsertion	low	8.1	26	508	54.2	4.6	11.3	59.7	47.5	1000	0
29	1347055	SD	N	CVCInsertion	low	9	12	18	16.2	1.48	2.1	59.4	38.2	0	1SDP
30	1385975	RS	N	Ascitic Tap	low	8.9	8.5	41	27.2	2.47	4.8	40.4	26.3	1000	1SDP
31	1300462	GS	N	CVCInsertion	low	9.4	3.1	66	52.1	4.6	5.2	33.3	23.4	1250	0
32	1135946	BS	N	EVL	high	9	3	40	32.2	2.92	2.8	45.2	26.6	750	1SDP
33	477218	VS	N	CVCInsertion	low	8.9	7	40	35.4	3.21	5	46.1	30.5	750	1SDP

SR. NO.	MRD NO	INTIALS	CCT Total cost of transfusion in Rs.	CCTNet Cost in Rs.	CCT Bleeding event	CCT Transfusion related side-effect	TEG Total amount of FFP Infused, mL	TEG Total amount of PLTs Infused, Units	TEG Total cost of transfusion in Rs.	TEG Net Cost in Rs.	TEG Bleeding event(ml)	POST PROCEDURE HEMOGLOBIN (gm/dl)	TEG Transfusion related side-effect
1	1350891	ZS	4800	5130	No	No	0	0	0	5100	No	9.9	No
2	1364569	NS	17500	17830	No	No	0	0	0	5100	No	8.5	No
3	37571	M	17500	17830	No	No	0	0	0	5100	100	11.1	No
4	1359972	TS	6000	6330	No	No	0	0	0	5100	No	8.2	No
5	904278	S	4800	5130	No	No	0	1SDP	12700	17800	No	8.8	No
6	1361585	MS	16300	16630	No	No	0	0	0	5100	No	11.6	No
7	1067008	DS	12700	13030	No	No	0	1SDP	12700	17800	No	9.8	No
8	1364573	AS	12700	13030	No	No	0	1SDP	12700	17800	No	12.5	No
9	1313028	SS	18700	19030	No	No	0	1SDP	12700	17800	No	11	No
10	1221385	VS	7200	7530	No	No	0	0	0	5100	200	11.8	No
11	1366841	KG	4800	5130	No	No	0	0	0	5100	No	12.1	No
12	1375472	MK	6000	6330	No	No	0	0	0	5100	No	7.8	No
13	1345507	PS	17500	17830	No	No	0	1SDP	12700	17800	1000	7	No
14	1401163	RK	16300	16630	No	No	0	1SDP	12700	17800	No	8.6	No
15	1407588	LS	17500	17830	No	No	0	1SDP	12700	17800	No	8.2	No
16	1286113	G	4800	5130	No	No	0	0	0	5100	No	8	No
17	944068	JS	4800	5130	No	No	0	0	0	5100	No	9	No
18	1411001	KK	6000	6330	No	No	0	0	0	5100	No	11	No
19	1384499	SS	4800	5130	No	No	1000	1SDP	17500	22600	No	8.3	No
20	27889	GS	17500	17830	No	No	0	1SDP	12700	17800	No	12.1	No
21	1300562	GS	4800	51300	No	No	0	1SDP	12700	17800	No	9.5	No
22	1402470	MS	17500	17830	No	No	0	1SDP	12700	17800	No	10	No
23	1338123	JS	4800	5130	No	No	0	0	0	5100	No	10.2	No
24	1379311	VK	4800	5130	No	No	0	1SDP	12700	17800	No	9.9	No
25	1313128	SS	4800	5130	No	No	0	1SDP	12700	17800	No	7.8	No
26	1385601	LK	16300	16630	No	No	0	0	0	5100	No	10.7	No
27	1383118	NS	17500	17830	No	No	0	0	0	5100	No	8.8	No
28	1402058	LS	4800	5130	No	No	0	0	0	5100	No	8.1	No
29	1347055	SD	12700	13030	No	No	0	1SDP	12700	17800	No	9	No
30	1385975	RS	17500	17830	No	No	0	1SDP	12700	17800	No	8.7	No
31	1300462	GS	6000	6330	No	No	0	1SDP	12700	17800	No	9.4	No
32	1135946	BS	16300	16630	No	No	0	1SDP	12700	17800	No	9	No
33	477218	VS	16300	16630	No	No	0	1SDP	12700	17800	No	8.8	No

SR. NO.	MRD NO	INTIALS	AGE (Year)	GENDER	AGE GROUP	ADDRESS	CONTACT NO	BODY WEIGHT (Kg)	IDEAL BODY WEIGHT (Kg)	ETILOGY	ASCITES	HEPATIC ENCEPHALOPATHY	MELD SCORE	CHILD PUGH CLASS
34	1415216	JS	45	M	2	Barnala	9878793014	72	70	Alcholic Liver Disease	grade 3	grade3	29	C
35	1313270	RS	62	M	4	Moga	78890517	94	68.4	Alcholic Liver Disease	grade 2	-	20	C
36	1404088	RS	23	M	1	Fazilka	9417181788	70	68.4	Autoimmune Liver Disease	grade 2	grade3	21	C
37	1311083	NB	55	M	3	Ludhiana	8264240947	50	-	Alcholic Liver Disease	grade 1	grade2	12	C
38	1296851	GS	58	M	3	Moga	9814413735	84	80	Alcholic Liver Disease	grade 3	-	22	C
39	132170	MS	57	M	3	Moga	9874551256	72	68.4	Alcholic Liver Disease	grade 2	grade1	15	C
40	1419171	R	40	M	1	Udhampur	9858122497	80	75	Alcholic Liver Disease	grade 3	grade3	21	C
41	249432	GD	66	F	4	Ludhiana	9888764231	66.8	-	Metabolic associated steatotic liver disease	-	-	13	A
42	1397083	PG	60	M	3	J &K	9593976565	71	70.7	Alcholic Liver Disease	grade 2	-	15	B
43	1426089	TS	37	M	1	Bathinda	9653741000	76	68.4	Alcholic Liver Disease	grade 3	grade1	34	C
44	867964	BS	54	M	3	Fazilka	9417217052	80	68.4	Alcholic Liver Disease	grade 2	-	15	B
45	1350934	RK	56	F	3	Amritsar	9842345239	65	59	Metabolic associated steatotic liver disease	grade 2	grade3	15	B
46	228296	SS	70	M	4	Gurdaspur	9855143519	73	-	Alcholic Liver Disease	grade 1	-	30	C
47	1412563	MS	55	M	3	Gurdaspur	9914315293	84	61	Alcholic Liver Disease	grade 3	-	26	C
48	1226453	RP	34	M	1	Pathankot	9569581499	75	-	Alcholic Liver Disease	-	-	15	B
49	1429819	JS	42	M	2	Bathinda	9877844954	95	84.5	Alcholic Liver Disease	grade 3	grade2	46	C
50	1398371	AS	38	M	1	Sangrur	9855245430	68	54.6	Alcholic Liver Disease	grade 3	grade3	23	C
51	1550645	GPS	62	M	4	Gobindgarh	8146990375	90	80	Alcholic Liver Disease	grade 2	-	13	C
52	813734	VG	45	M	2	J&K	9006736241	50	-	Alcholic Liver Disease	grade 1	-	29	B
53	180585	AK	60	M	3	Ludhiana	9781692424	60	-	Alcholic Liver Disease	grade 2	-	24	C
54	1546967	VS	50	M	2	J & K	9622161085	85	75	Alcholic Liver Disease	grade 2	grade2	22	C
55	684329	SS	57	M	3	Patiala	9815062861	75	-	Alcholic Liver Disease	-	grade3	29	C
56	1186735	J	65	M	4	Jalandhar	9417040636	60	57	Alcholic Liver Disease	grade 3	grade2	42	C
57	1562386	RR	45	M	2	Budhlada	7889231194	60	57	Alcholic Liver Disease	grade 3	-	26	C
58	1564422	NK	28	M	1	Ludhiana	9814762271	70	66	Alcholic Liver Disease	grade 2	-	36	C
59	1506256	SS	60	M	3	Mohali	9476207118	60	-	Alcholic Liver Disease	grade 3	-	29	C
60	1560280	SS	43	M	2	Patiala	7973457969	60	55	Alcholic Liver Disease	grade 2	grade2	37	C
61	1558377	RS	46	M	2	J & K	6005453426	50	-	Metabolic associated steatotic liver disease	-	grade2	23	C
62	1572326	KD	40	M	1	Ludhiana	9815619019	90	-	Metabolic associated steatotic liver disease	grade 1	grade2	42	C
63	1041117	CS	48	M	2	J & K	6006295829	90	-	Alcholic Liver Disease	grade 1	grade2	27	C
64	1517213	AK	24	M	1	Ludhiana	9988012192	60	54.6	Metabolic associated steatotic liver disease	grade 2	grade1	23	C
65	1157687	Y	59	M	3	HP	9816764965	63	54	Alcholic Liver Disease	grade 3	-	31	C

SR. NO.	MRD NO	INTIALS	HCC	PROCEDURE	RISK OF BLEEDING	HEMOGLOBIN (gm/dl)	WBC (10^3/ul)	PLATELET COUNT (10^3 /Ul)	PTI	INR	TEG R VALUE (Mins)	TEG Alpha Angle (Degree)	TEG Max Amplitude (MM)	CCT Total amount of FFP Infused, mL	CCT Total amount of PLTs Infused, Units
34	1415216	JS	N	DCInsertion	low	9	9.6	198	51.2	4	7	49.5	47.4	1000	0
35	1313270	RS	N	PCD Insertion (Pleural effusion)	high	9.9	5.3	69	19.2	1.75	1.6	65.1	36.9	1000	0
36	1404088	RS	N	Ascitic Tap	low	10.6	7.6	36	31.4	2.84	5.7	30.1	39.6	1000	1SDP
37	1311083	NB	N	DCInsertion	low	8.3	54	16	32.8	2.98	11.8	19.2	19.6	750	1SDP
38	1296851	GS	N	CVCInsertion	low	8.3	2.1	16	19.2	1.75	1.7	27.6	20.1	1250	1SDP
39	132170	MS	N	CVCInsertion	low	10	8	40	19.2	1.75	4.8	59.6	29	1000	1SDP
40	1419171	R	N	CVCInsertion	low	8.6	9.5	27	18.1	1.65	9.2	24.6	19	1250	1SDP
41	249432	GD	N	CVCInsertion	low	11.3	12.8	20	12.7	1.6	0.2	86.9	61.5	1000	1SDP
42	1397083	PG	N	CVCInsertion	low	8.2	11.5	16	38	3.44	3.2	48.4	37.5	1000	1SDP
43	1426089	TS	N	EVL	high	8.3	7.7	120	25.6	2.33	1.5	53.1	27.8	1000	0
44	867964	BS	N	CVCInsertion	low	10.3	12.3	120	56	5.05	3.5	68.3	35.8	1000	0
45	1350934	RK	N	Ascitic Tap	low	8.8	9.4	40	62.1	5.6	4.2	50.6	40.8	1000	1SDP
46	228296	SS	N	PCD Insertion (Pleural effusion)	high	8.1	6.8	88	27.1	2.46	2.2	70.3	44.2	1000	0
47	1412563	MS	N	EVL	high	9	12.5	86	27.1	2.46	4	41.8	24.6	1000	0
48	1226453	RP	N	CVCInsertion	low	10.7	3.3	22	18.8	1.72	4.1	48.5	34.6	1250	1SDP
49	1429819	JS	N	DCInsertion	low	11.6	21.6	72	40.1	3.63	6.6	30	34.3	1250	0
50	1398371	AS	N	Ascitic Tap	low	8.5	5.25	42	33.9	3.08	7.3	30.6	24.6	750	1SDP
51	1550645	GPS	N	ERCP	high	13.4	10	202	19.5	1.78	7	55	57.5	1000	0
52	813734	VG	Y	CVCInsertion	low	11.3	10	20	23.6	2.15	6.5	61.5	59.8	750	1SDP
53	180585	AK	N	EVL	high	12.3	15.5	90	26.1	2.37	3.5	72.7	56.5	1000	0
54	1546967	VS	N	CVCInsertion	low	8.2	7.39	16	18.6	1.7	2	64.7	33.5	1000	1SDP
55	684329	SS	N	CVCInsertion	low	8.2	8.99	60	35.6	3.23	1.6	71.9	42.1	1250	0
56	1186735	J	N	Lymph node biopsy (mesenteric lymph node)	high	8.6	10.5	248	72.8	6.55	6.2	69.1	45.1	750	0
57	1562386	RR	N	PCD Insertion (Pleural effusion)	high	10.4	24.6	140	30	2.72	4.5	57.3	50.8	750	0
58	1564422	NK	N	CVCInsertion	low	10	30.5	126	49.2	4.45	9.8	49.4	52.9	1000	0
59	1506256	SS	N	EVL	high	8.7	5.5	85	24.7	2.25	5.7	42.3	37.2	1000	0
60	1560280	SS	N	DCInsertion	low	10.6	4.75	24	16	1.46	1.8	64.6	37.9	0	1SDP
61	1558377	RS	N	CVCInsertion	low	10	10	146	41.8	3.78	7	60.9	62.2	750	0
62	1572326	KD	N	DCInsertion	low	8.5	13	150	31.1	3.8	9.2	46	40	1250	0
63	1041117	CS	N	CVCInsertion	low	8.5	10.8	48	23	2.09	4.2	61.3	62.8	1250	1SDP
64	1517213	AK	N	CVCInsertion	low	10	1.8	24	25.7	2.39	5.9	44.6	47.5	750	1SDP
65	1157687	Y	N	EVL	high	11.6	11.3	62	50.4	4.55	4.3	57.5	49.8	750	0

SR. NO.	MRD NO	INTIALS	CCT Total cost of transfusion in Rs.	CCTNet Cost in Rs.	CCT Bleeding event	CCT Transfusion related side-effect	TEG Total amount of FFP Infused, mL	TEG Total amount of PLTs Infused, Units	TEG Total cost of transfusion in Rs.	TEG Net Cost in Rs.	TEG Bleeding event(ml)	POST PROCEDURE HEMOGLOBIN (gm/dl)	TEG Transfusion related side-effect
34	1415216	JS	4800	5130	No	No	0	0	0	5100	No	9	No
35	1313270	RS	4800	5130	No	No	0	1SDP	12700	17800	No	9.7	No
36	1404088	RS	17500	17830	No	No	0	1SDP	12700	17800	No	10.5	No
37	1311083	NB	16300	16630	No	No	0	1SDP	12700	17800	No	8.4	No
38	1296851	GS	18700	19030	No	No	0	1SDP	12700	17800	No	8	No
39	132170	MS	17500	17830	No	No	0	1SDP	12700	17800	No	10.1	No
40	1419171	R	18700	19030	No	No	0	1SDP	12700	17800	No	8.7	No
41	249432	GD	17500	17830	No	No	0	0	0	5100	No	11.2	No
42	1397083	PG	17500	17830	No	No	0	1SDP	12700	17800	No	8.3	No
43	1426089	TS	4800	5130	No	No	0	1SDP	12700	17800	No	8.2	No
44	867964	BS	4800	5130	No	No	0	1SDP	12700	17800	No	10.4	No
45	1350934	RK	17500	17830	No	No	0	1SDP	12700	17800	No	8.8	No
46	228296	SS	4800	5130	No	No	0	0	0	5100	No	8.2	No
47	1412563	MS	4800	5130	No	No	0	1SDP	12700	17800	No	9.1	No
48	1226453	RP	18700	19030	No	No	0	1SDP	12700	17800	No	10.5	No
49	1429819	JS	6000	6330	No	No	0	1SDP	12700	17800	No	11.5	No
50	1398371	AS	16300	16630	No	No	0	1SDP	12700	17800	No	8.4	No
51	1550645	GPS	4800	5130	No	No	0	0	0	5100	No	13.5	No
52	813734	VG	16300	16630	No	No	0	0	0	5100	50	11.2	No
53	180585	AK	4800	5130	No	No	0	0	0	5100	No	12	No
54	1546967	VS	17500	17830	No	No	0	1SDP	12700	17800	No	8.1	No
55	684329	SS	6000	6330	No	No	0	0	0	5100	No	8.3	No
56	1186735	J	3600	3930	No	No	0	0	0	5100	No	8.4	No
57	1562386	RR	3600	3930	No	No	0	0	0	5100	No	10.3	No
58	1564422	NK	4800	5130	No	No	0	0	0	5100	No	10.1	No
59	1506256	SS	4800	5130	No	No	0	0	0	5100	No	8.8	No
60	1560280	SS	12700	13030	No	No	0	1SDP	12700	17800	No	10.5	No
61	1558377	RS	3600	3960	No	No	0	0	0	5100	No	10.1	No
62	1572326	KD	6000	6330	No	No	0	1SDP	12700	17800	No	8.6	No
63	1041117	CS	18700	19030	No	No	0	0	0	5100	No	8.5	No
64	1517213	AK	16300	16630	No	No	0	0	0	5100	No	10.2	No
65	1157687	Y	3600	3930	No	No	0	0	0	5100	No	11.4	No

SR. NO.	MRD NO	INTIALS	AGE (Year)	GENDER	AGE GROUP	ADDRESS	CONTACT NO	BODY WEIGHT (Kg)	IDEAL BODY WEIGHT (Kg)	ETILOGY	ASCITES	HEPATIC ENCEPHALOPATHY	MELD SCORE	CHILD PUGH CLASS
66	1568304	VDS	68	M	4	HP	8628881999	60	52.3	Alcholic Liver Disease	grade 2	-	26	C
67	1304361	VS	61	M	4	Amritsar	9781812340	50	54	Alcholic Liver Disease	grade 3	grade1	26	C
68	1398440	GS	33	M	1	Patiala	9478101122	60	54	Alcholic Liver Disease	grade 3	grade2	29	C
69	1255122	JP	60	M	3	Ludhiana	9781935009	70	-	Alcholic Liver Disease	-	grade2	16	B
70	49819	AK	53	M	3	Amritsar	7844039000	86	68.4	Metabolic associated steatotic liver disease	grade 2	grade1	24	C
71	1583771	AS	38	M	1	Fazilka	9855347900	60	54	Alcholic Liver Disease	grade 2	-	24	C
72	1575990	JS	60	M	3	Gurdaspur	9872154042	60	66	Alcholic Liver Disease	grade 2	-	43	C
73	1421964	M	53	M	3	Rajesthan	9872154041	60	-	Alcholic Liver Disease	-	-	16	B
74	1341598	SS	66	M	4	Hoshiarpur	9417765480	70	66	Alcholic Liver Disease	grade 3	-	18	B
75	1590747	VM	71	F	4	Amritsar	7009269868	90	57	Metabolic associated steatotic liver disease	grade 3	-	27	C
76	1205989	SC	68	M	4	Sirsa	9992371184	58	-	Metabolic associated steatotic liver disease	grade 1	grade2	34	C
77	1458256	SS	38	M	1	Moga	9814644398	59	66	Alcholic Liver Disease	grade 3	-	24	C
78	1595675	SS	55	M	3	J & K	8427104958	65	64	Alcholic Liver Disease	grade 2	grade2	37	C
79	1578831	DK	42	M	2	J & K	7889981249	50	-	Alcholic Liver Disease	-	grade2	33	C
80	1598056	AS	47	M	2	HP	9864236211	60	56.9	Alcholic Liver Disease	grade 3	grade1	18	B
81	1598359	AK	75	F	4	Ludhiana	8872461151	58	50.1	Hepatitis C	grade 3	-	26	C
82	1599612	GS	31	M	1	Ferozepur	9781368098	85	-	Alcholic Liver Disease	grade 1	grade2	22	C
83	1603962	PG	51	M	3	J & K	7006130438	70	-	Alcholic Liver Disease	-	-	18	B
84	1491802	MS	40	M	1	Amritsar	9779765665	67	-	Alcholic Liver Disease	-	-	18	C
85	1602388	RS	30	M	1	Sangrur	8437992823	50	-	Alcholic Liver Disease	-	-	23	C
86	1118444	PDK	74	M	4	J & K	9419101129	60	64	Metabolic associated steatotic liver disease	grade 2	grade3	23	C
87	1568922	Z	65	F	4	J & K	9906309003	74	60	Metabolic associated steatotic liver disease	grade 3	grade2	20	C
88	1611853	SS	55	M	3	Karnal	9813983911	90	-	Alcholic Liver Disease	-	-	12	A
89	27962	AS	58	M	3	Rajasthan	9413613623	91	75.3	Alcholic Liver Disease	grade 2	grade2	25	C
90	1589468	MK	54	M	3	Jalandhar	9463030413	72	62	Alcholic Liver Disease	grade 3	-	29	C
91	1458856	S	49	M	2	Mohali	9854763241	60	-	Alcholic Liver Disease	grade 3	grade3	30	C
92	1568357	HK	50	M	2	Amritsar	9874562313	62	-	Metabolic associated steatotic liver disease	grade 2	-	20	C
93	1616213	PS	60	M	3	Fazilka	9874624651	75	-	Alcholic Liver Disease	grade 2	grade2	24	C
94	1617856	DS	48	M	2	Gurdaspur	9876599401	78	66	Alcholic Liver Disease	grade 2	-	49	C
95	1615351	BS	43	M	2	J & K	9419201839	75	66	Alcholic Liver Disease	grade 2	grade2	24	C
96	1619783	AS	41	M	2	J & K	9419133018	55	62	Alcholic Liver Disease	grade 3	-	19	C
97	586000	GL	66	M	4	J & K	7829826672	73	55	Alcholic Liver Disease	grade 3	-	14	C

SR. NO.	MRD NO	INTIALS	HCC	PROCEDURE	RISK OF BLEEDING	HEMOGLOBIN (gm/dl)	WBC (10^3/ul)	PLATELET COUNT (10^3 /Ul)	PTI	INR	TEG R VALUE (Mins)	TEG Alpha Angle (Degree)	TEG Max Amplitude (MM)	CCT Total amount of FFP Infused, mL	CCT Total amount of PLTs Infused, Units
66	1568304	VDS	Y	PCD Insertion (Pleural effusion)	high	11.2	8.7	142	27.2	2.47	7.4	36.1	47.8	750	0
67	1304361	VS	N	EVL	high	11	5.6	56	25.4	2.31	5.9	45.8	36.7	750	0
68	1398440	GS	N	Ascitic Tap	low	8.2	2.8	22	32.8	2.98	4.8	38.3	27	750	1SDP
69	1255122	JP	N	Incision & Drainage	high	9.8	11.6	72	18.5	1.69	3.4	64.6	52	1000	0
70	49819	AK	N	EVL	high	8	6.3	90	33	3.02	3.2	63.4	46.7	1000	0
71	1583771	AS	N	CVCInsertion	low	10.6	18	26	29.1	2.64	9.7	64.3	47.6	750	1SDP
72	1575990	JS	N	Ascitic Tap	low	10.8	23	177	50.4	4.6	2.8	20.9	64	1000	0
73	1421964	M	N	Hernia Repair	high	10.7	8.1	98	21.5	1.96	4	64.8	51.3	1000	0
74	1341598	SS	N	EVL	high	8.3	3.63	62	17.3	1.62	8.8	43.4	38.2	1000	0
75	1590747	VM	N	CVCInsertion	low	11.3	20	20	26.8	2.44	3.7	50.2	34.9	750	1SDP
76	1205989	SC	N	CVCInsertion	low	9.2	4.9	16	25.8	2.35	7.6	32.4	31.2	1000	1SDP
77	1458256	SS	N	CVCInsertion	low	8.4	0.9	30	31.1	2.82	4	61.2	54	1000	1SDP
78	1595675	SS	N	EVL	high	8.1	5.7	20	22.3	2.03	5.9	61.5	47.5	1000	1SDP
79	1578831	DK	N	CVCInsertion	low	8	8.9	132	50.3	4.5	2.3	62.1	46.7	750	0
80	1598056	AS	N	ERCP	high	10.6	15.9	119	17.5	1.6	9.3	50.7	57.5	750	0
81	1598359	AK	N	CVCInsertion	low	8.3	8.04	40	22.2	2.02	7.4	47.9	43.8	750	1SDP
82	1599612	GS	N	DCInsertion	low	10.9	20.2	30	33	2.99	8.3	51.1	44.7	1250	1SDP
83	1603962	PG	N	EVL	high	12	3.45	46	17.9	1.63	4.5	50.3	42.3	1000	1SDP
84	1491802	MS	N	ERCP	high	13	3.5	50	20.8	1.9	5.4	62.8	32.4	1000	0
85	1602388	RS	N	CVCInsertion	low	11.7	18	42	22.1	2.01	5.3	66.6	47.04	750	1SDP
86	1118444	PDK	N	EVL	high	12	7.3	72	20.3	1.85	3.5	62.5	41.5	1000	0
87	1568922	Z	N	CVCInsertion	low	9.3	6.1	34	19.3	1.76	5.8	53.3	38	1000	1SDP
88	1611853	SS	N	EVL	high	8	8.5	44	16	1.46	3.2	64.6	45.8	1250	1SDP
89	27962	AS	N	Debridement of Leg Cellulitis	high	8	8.6	92	17	1.55	2.2	70.8	52.3	1250	0
90	1589468	MK	N	Ascitic Tap	low	12	7.9	150	34.2	3.1	5.2	69.2	55.6	1000	0
91	1458856	S	N	DCInsertion	low	9.4	10.4	94	40.6	3.68	4	61.2	54.3	1000	0
92	1568357	HK	N	PCD Insertion (Pleural effusion)	high	8.2	16.4	164	18.8	1.72	7.2	63.5	56.5	1000	0
93	1616213	PS	N	CVCInsertion	low	8.9	5.3	42	30.6	2.78	3.7	28.1	38.9	1250	1SDP
94	1617856	DS	N	DCInsertion	low	8.5	12.1	80	51.4	4.64	1.2	39.4	6.5	1000	0
95	1615351	BS	N	Ascitic Tap	low	8.2	9.2	30	32.1	2.91	4.3	59.7	45	1000	1SDP
96	1619783	AS	N	CVCInsertion	low	11.1	22	280	52.1	4.5	5.3	55.1	45.1	1000	0
97	586000	GL	N	Ascitic Tap	low	8	14.4	176	53.1	4.6	5.4	73.9	64.9	750	0

SR. NO.	MRD NO	INTIALS	CCT Total cost of transfusion in Rs.	CCTNet Cost in Rs.	CCT Bleeding event	CCT Transfusion related side-effect	TEG Total amount of FFP Infused, mL	TEG Total amount of PLTs Infused, Units	TEG Total cost of transfusion in Rs.	TEG Net Cost in Rs.	TEG Bleeding event(ml)	POST PROCEDURE HEMOGLOBIN (gm/dl)	TEG Transfusion related side-effect
66	1568304	VDS	3600	3930	No	No	0	0	0	5100	No	11.1	No
67	1304361	VS	3600	3930	No	No	0	0	0	5100	No	11.2	No
68	1398440	GS	16300	16630	No	No	0	1SDP	12700	17800	No	8.1	No
69	1255122	JP	4800	5130	No	No	0	0	0	5100	No	9.8	No
70	49819	AK	4800	5130	No	No	0	0	0	5100	No	8.1	No
71	1583771	AS	16300	16630	No	No	0	0	0	5100	No	10.5	No
72	1575990	JS	4800	5130	No	No	0	0	0	5100	No	10.8	No
73	1421964	M	4800	5130	No	No	0	0	0	5100	No	10.7	No
74	1341598	SS	4800	5130	No	No	0	1SDP	12700	17800	No	8.3	No
75	1590747	VM	16300	16630	No	No	0	1SDP	12700	17800	No	11.4	No
76	1205989	SC	17500	17830	No	No	0	1SDP	12700	17800	No	9.1	No
77	1458256	SS	17500	17830	No	No	0	0	0	5100	No	8.3	No
78	1595675	SS	17500	17830	No	No	0	0	0	5100	No	8.2	No
79	1578831	DK	3600	3930	No	No	0	0	0	5100	No	8	No
80	1598056	AS	3600	3930	No	No	0	0	0	5100	No	10.5	No
81	1598359	AK	16300	16630	No	No	0	0	0	5100	No	8.4	No
82	1599612	GS	18700	19030	No	No	0	0	0	5100	No	10.8	No
83	1603962	PG	17500	17830	No	No	0	0	0	5100	No	12.1	No
84	1491802	MS	4800	5130	No	No	0	1SDP	12700	17800	75	12.9	No
85	1602388	RS	16300	16630	No	No	0	0	0	5100	No	11.6	No
86	1118444	PDK	4800	5130	No	No	0	0	0	5100	No	11.9	No
87	1568922	Z	17500	17830	No	No	0	1SDP	12700	17800	No	9.2	No
88	1611853	SS	18700	19030	No	No	0	0	0	5100	No	8.1	No
89	27962	AS	6000	6330	No	No	0	0	0	5100	100	8	No
90	1589468	MK	4800	5130	No	No	0	0	0	5100	No	12.1	No
91	1458856	S	4800	5130	No	No	0	0	0	5100	No	9.2	No
92	1568357	HK	4800	5130	No	No	0	0	0	5100	No	8.1	No
93	1616213	PS	18700	19030	No	No	0	1SDP	12700	17800	No	8.8	No
94	1617856	DS	4800	5130	No	No	0	1SDP	12700	17800	No	8.6	No
95	1615351	BS	17500	17830	No	No	0	0	0	5100	No	8.3	No
96	1619783	AS	4800	5130	No	No	0	0	0	5100	No	11	No
97	586000	GL	3600	3930	No	No	0	0	0	5100	No	8.1	No

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The Principal
Dayanand Medical College & Hospital
Ludhiana

Subject:: Approval of Plan of Thesis.

This is to inform you that the Faculty of Medical Sciences in its meeting held on 25.09.2023 has approved the plan of thesis of **Khiati Goyal**, a student of your college for **MD General Medicine** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis
To study the role of thromboelastography (Teg) in correction of coagulopathy in patients of cirrhosis undergoing invasive procedures .

Supervisor	**Co-Supervisor:-**	**Co-Supervisor:-**
Dr. Vandana Midha	Dr. Ajit Sood	Dr. Ramit Mahajan
Professor	Prof. & Head	Assoc. Professor
Dept. of Medicine	Dept. of Gastroenterology	Dept. of Gastroenterology

The student may submit the thesis in triplicate alongwith the plan in triplicate also, to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She may be directed to attach a photocopy of this letter with the forwarding letter while submitting thesis in the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic, if any.

Controller of Examinations

Note :

1. *If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.*

SCAN AnyScanner

TO STUDY THE ROLE OF THROMBOELASTOGRAPHY (TEG) IN CORRECTION OF COAGULOPATHY IN PATIENTS OF CIRRHOSIS UNDERGOING INVASIVE PROCEDURES THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED IN

PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MD

IN

GENERAL MEDICINE

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

JULY, 2022

Dr. KHIATI GOYAL

DEPARTMENT OF GENERAL MEDICINE
DAYANAND MEDICAL COLLEGE AND HOSPITAL
LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	TO STUDY THE ROLE OF THROMBOELASTOGRAPHY (TEG) IN CORRECTION OF COAGULOPATHY IN PATIENTS OF CIRRHOSIS UNDERGOING INVASIVE PROCEDURES
For the degree of	MD General Medicine
Name of the candidate	Dr. Khiati Goyal
Supervisor	Dr. Vandana Midha, Professor, Department of Medicine, DMCH, Ludhiana
Co-Supervisor	Dr Ajit Sood, Professor & Head, Department of Gastroenterology, DMCH, Ludhiana Dr Ramit Mahajan, Associate Professor, Department of Gastroenterology, DMCH, Ludhiana
Institution	Dayanand Medical College and Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

INTRODUCTION: Thromboelastography (TEG) is a rapid global assessment tool of hemostasis using whole blood, allowing for effective quantification of platelet function, thrombus formation, clot tensile strength, and fibrinolysis.

AIMS AND OBJECTIVE

To assess the role of TEG in patients in defining product requirement for achieving haemostasis in comparison to Conventional Coagulation Test (PTI/INR and platelets) in patient with cirrhosis who are undergoing surgery or radiological interventions.

MATERIAL AND METHODS

In patient department and Out patient department record of patients of General Medicine, Gastroenterology ,Cardiology ,Surgery and Intervention Radiology at Dayanand Medical College and Hospital, Ludhiana.

METHOD OF COLLECTION OF DATA

Cases shall be selected on the basis of criteria set in inclusion and exclusion criteria for the study and TEG shall be performed in selected patients.

CLINICAL SIGNIFICANCE

The patients with CLD have a rebalanced coagulation state ., CCTs are routinely performed in this patient group and are commonly used to guide clinical decisions such as blood product administration. 6 Unlike CCTs, TEG uses the principle of viscoelasticity to measure coagulation initiation, clot formation, clot strength, and fibrinolysis, providing a global assessment of hemostatic function. TEG may avoid unnecessary blood products transfusion in patients with cirrhosis and significant coagulopathy as defined by conventional coagulation tests undergoing invasive procedures, hence reducing the cost spent on blood/blood product transfusion and the risk of transfusion related complications

Keywords: Thromboelastography, cirrhosis, blood products

(Signature)	(Signature)	(Signature)	(Signature)	(Signature)
Candidate	Co-supervisor	Co-supervisor	Supervisor	Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"TO STUDY THE ROLE OF THROMBOELASTOGRAPHY (TEG) IN CORRECTION OF COAGULOPATHY IN PATIENTS OF CIRRHOSIS UNDERGOING INVASIVE PROCEDURES"** exist in the Department of General Medicine at Dayanand Medical College and Hospital, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis are genuine and is collected by the candidate herself under our supervision and guidance.

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Place : Ludhiana

Date : 22/9/22

APPROVAL PROFORMA
BY
RESEARCH & ETHICAL COMMITTEE
DAYANAND MEDICAL COLLEGE & HOSPITAL, LUDHIANA

Name of candidate	Dr Khiati Goyal
Department	General Medicine
Topic of Thesis	TO STUDY THE ROLE OF THROMBOELASTOGRAPHY (TEG) IN CORRECTION OF COAGULOPATHY IN PATIENTS OF CIRRHOSIS UNDERGOING INVASIVE PROCEDURES
Likely date of appearing in PG examination	MAY, 2024
Date of enrollment	MARCH 7, 2022
Name of Head of Department	Dr Dinesh Gupta
1) Supervisor **2) Co-Supervisor**	Dr Vandana Midha Dr Ajit Sood Dr. Ramit Mahajan
Signature of Members of Research Committee with Stamp	**Signature of Members of Ethics Committee with Stamp**
Dr. Harpreet Kaur (Professor & Head, Pathology)	Mr. R K Sharma (Legal Expert)
Dr. Jaspal Singh (Professor & Head, Surgery)	Dr. Ramit Mahajan (Associate Professor, Gastroenterology)
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Dr. Sandeep Kaushal (Dean Academics & Professor & Head, Pharmacology)	Dr. Sandeep Kaushal (Dean Academics & Professor & Head, Pharmacology)
Dr. Gurpreet S Wander (Vice Principal)	Dr. Gurpreet S Wander (Vice Principal & Professor & Head, Cardiology)
	Dr. Gagandeep Singh (Secretary, Ethics Committee Professor & Head, Neurology)

Approved: Yes / ~~No~~

Dr. Sandeep Puri
Chairperson
Research Committee

Chairperson
Research Committee

Approved: Yes / ~~No~~

Prof. Arvind Malhotra
Chairperson
Ethics Committee

Chairperson
Ethics Committee

BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT
PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

1	NAME OF THE CANDIDATE AND ADDRESS	DR. KHIATI GOYAL
2	NAME OF THE INSTITUTE	DAYANAND MEDICAL COLLEGE AND HOSPITAL
3	COURSE OF STUDY AND SUBJECT	M.D. GENERAL MEDICINE
4	DATE OF ADMISSION OF COURSE	07/03/2022
5	TITLE OF THE TOPIC	TO STUDY THE ROLE OF THROMBOELASTOGRAPHY (TEG) IN CORRECTION OF COAGULOPATHY IN PATIENTS OF CIRRHOSIS UNDERGOING INVASIVE PROCEDURES

6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Thromboelastography (TEG) is a rapid global assessment tool of hemostasis using whole blood, allowing for effective quantification of platelet function, thrombus formation, clot tensile strength, and fibrinolysis.

The liver is essential to the maintenance of hemostasis.[1] Patients with severe chronic liver disease (CLD) who become acutely unwell and have to undergo various invasive diagnostic or therapeutic procedures may demonstrate several coagulation abnormalities as assessed by conventional coagulation tests (CCTs). Traditionally, such coagulation abnormalities have been considered to predict a higher risk of bleeding. However, more recently it has been proposed that patients with CLD have a *rebalanced coagulation state,* due to changes in both pro and antithrombotic mechanisms, whereby such patients are simultaneously at increased risk of thrombosis as well as bleeding.[2] In addition, a limitation of CCTs is that they are in vitro tests, which fail to capture the entirety of the in vivo coagulation system dysfunction in this population.[3,4] Despite such concerns however, CCTs are routinely performed in this patient group and are commonly used to guide clinical decisions such as blood product administration.

A potentially more physiologically relevant evaluation of coagulation status may be provided by thromboelastography (TEG).[5,6] Unlike CCTs, TEG uses the principle of viscoelasticity to measure coagulation initiation, clot formation, clot strength, and fibrinolysis, providing a global assessment of hemostatic function. Thromboelastography is a rapid, point-of-care test and is being increasingly used in cardiac surgery, trauma, and massive transfusions.[6,7]

TEG may avoid unnecessary blood products transfusion in patients with cirrhosis and significant coagulopathy as defined by conventional

coagulation tests undergoing invasive procedures hence reducing the cost spent on blood / blood product transfusion related complications.

Also, in developing countries like India, where resources are limited and patients have to pay for the health care facilities themselves, using TEG to guide blood product transfusion may save resources and also reduce financial burden on the patients.

6.2 REVIEW OF LITERATURE

Bleeding is a feared complication of invasive procedures in patients with cirrhosis. Pre-procedure use of fresh frozen plasma (FFP) and/or platelets (PLT) is common to prevent bleeding in cirrhotics.

The liver is responsible for the synthesis of many of the procoagulant and anticoagulant proteins responsible for maintaining hemostasis.[8] Liver dysfunction is often assumed to be associated with increased bleeding risk, but evidence suggests that other factors such as sepsis, hepatorenal syndrome, hypotension, and endothelial dysfunction contribute to this bleeding tendency rather than isolated cirrhosis and liver disease.[9,10] In most cases, a “rebalancing” occurs and the vast majority of chronic liver disease patients achieve a hemostatic equilibrium.[9,11-14] In cases of traumatic injury or prior to surgical procedures, the measured coagulopathy as assessed by INR is often reversed with pharmaceutical agents (e.g., vitamin K, prothrombin complex concentrate) or transfused blood products (e.g., plasma or platelets). Both PT and aPTT testing only evaluate a small number of pro-hemostatic proteins by mimicking clot formation in vitro and are not suitable to investigate acquired deficiency of both pro- and anticoagulants as occurs in cirrhosis. However, this practice of prophylactic transfusion to minimize the risk of hemorrhagic complications is not evidence based despite its wide acceptance.[11,12,14] Prophylactic transfusions expose the patient to increased risk of adverse events (e.g., transfusion reactions including transfusion-related acute lung injury [TRALI] and exacerbation of portal hypertension) as a result of the transfusion, while providing no protective effects.[12,15,16] PT and INR analyses assess isolated clotting pathways in vitro despite our knowledge that in vivo clotting pathways do not function in isolation.[17]

Viscoelastic haemostatic assays (VHAs) provide a global assessment of haemostasis by measuring the viscoelastic changes occurring during blood clotting, of which TEG is one of the most commonly used.

TEG is a point-of-care, global haemostasis assessment device that measures the viscoelastic changes that occur during the haemostatic process, providing real-time reports.[18]

A study by De Pietri et al.[19] compared TEG-guided blood product use with standard traditional measures in a randomized prospective trial. TEG-guided transfusion resulted in significantly lower transfusions without an increase in bleeding complications.

In a randomized controlled trial, Kumar et al.[20] evaluated a cohort of 96 patients with cirrhosis with nonvariceal bleeding. Patients were stratified into TEG-guided transfusion strategy or standard-of-care coagulation-based transfusion. The group in the TEG arm received significantly fewer blood product transfusions and had fewer adverse events related to transfusions.

Another study by De Pietri et al.'s[21] study supports following findings regarding the INR: The INR does not predict risk for procedure-related bleeding[22] and administration of FFP does not necessarily correct INR or reduce bleeding events. [23,24] Indicating that there are clear limitations in utilization of the INR in assessment of bleeding risk in liver disease.

PATHOPHYSIOLOGY

TEG is a non-invasive test that quantitatively measures the ability of whole blood to form a clot. The principle of this *in vitro* test is to detect and quantify dynamic changes of the viscoelastic properties of a blood sample during clotting under low shear stress. The test is performed in a specially designed system called a thromboelastograph. The system consists of 2 chambers simultaneously examining a blood sample in duplicate to reduce the risk of sampling and measurement errors. Each chamber consists of a platform with a disposable cup where a blood sample is placed and a detection pin suspended in its center. The cup oscillates around the detection pin in a limited arc of plus or minus (+/-) 4 degrees 45' every 5 seconds. Induced pin movement is recorded, and changes are measured as a function of time. Initially, there is little

movement of the pin since liquid blood possesses minimal viscosity, and the oscillations of the cup are not transmitted to the pin.

As the blood coagulates, it begins to adhere to both the cup and the pin, and movement of the cup induces motion on the pin. These gradually increasing viscoelastic mechanical properties of the blood reflect the developing 3-dimensional fibrin mesh and platelet components of the clot. The greater the viscoelasticity of the clot, the higher the amplitude of the pin motion. As fibrinolysis starts, the fibrin-platelet structure begins to dissolve gradually, and the clot loses its contact with the detection pin, which has less induced motion. The thromboelastogram is a graphical image of the recorded amplitude of movement of the pin as a function of time. Analytical software measures and quantifies these changes. Therefore, TEG measures the functional ability of the blood to make a hemostatic plug. A newer version replaces the cup rotation method with a resonance technique wherein the blood sample is subjected to vibration, and the vertical movement of the blood meniscus is measured under LED illumination. The system uses pre-measured cartridges that do not require pipetting and allows the simultaneous performance of four blood tests.

Specimen Requirements and Procedure

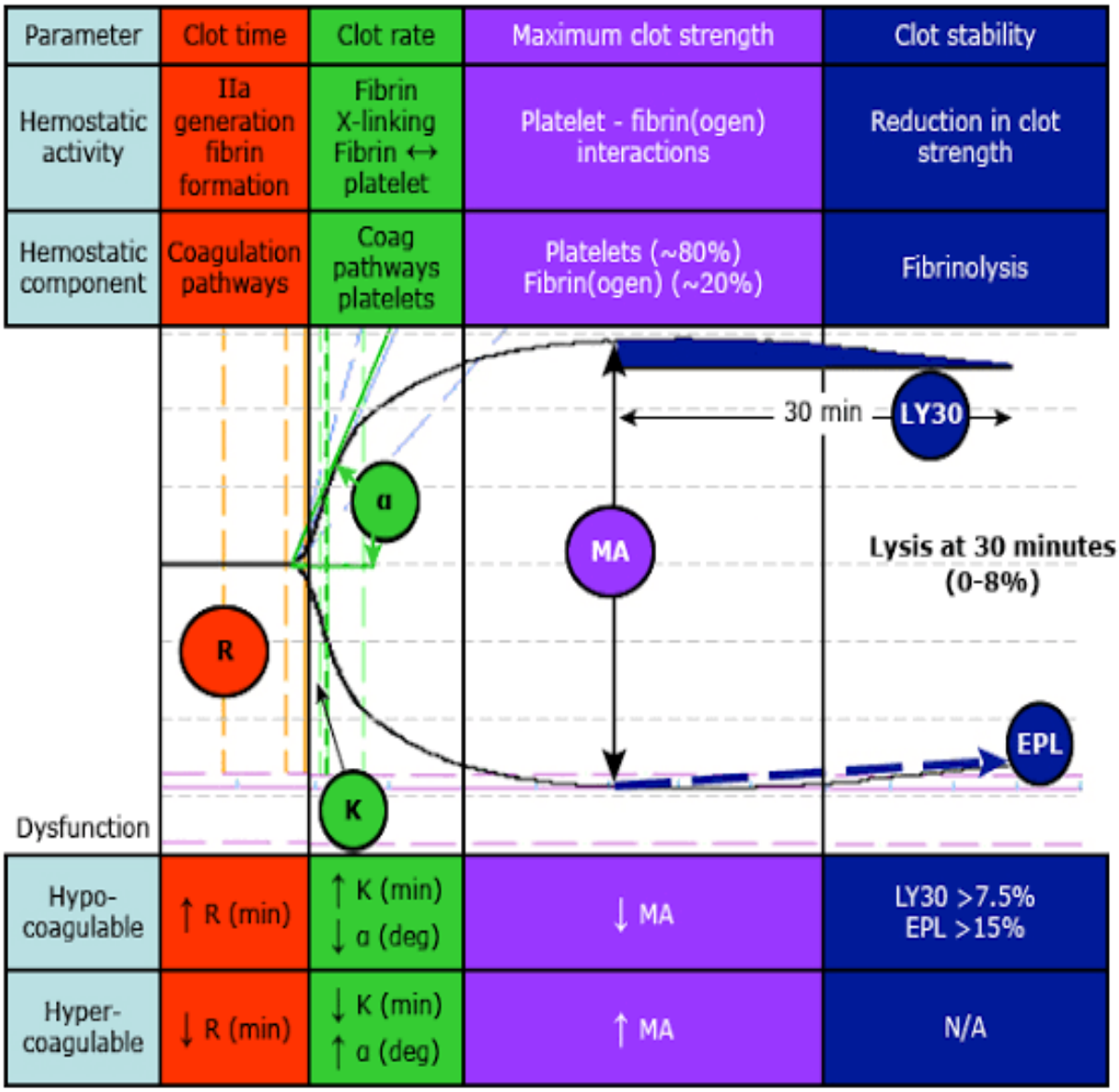
The blood sample is collected via venpuncture in a plastic vial with 3.2% buffered sodium citrate with a citrate-to-blood ratio of 1:9. The vial is inverted several times to mix the blood and citrate. Maintaining this citrate-blood ratio is crucial for test accuracy. Citrate binds calcium, an important cofactor of coagulation, preventing the blood from clotting before the beginning of the test. A clotted specimen, reflecting a vial overfilled with blood, cannot be used. For TEG testing, the collected non-clotted samples are considered stable and usable for up to 2 hours at room temperature. Non-citrated whole blood (native blood TEG or NATEM) can also be tested, but it must be used immediately. The test and reagents used are at room temperature. A volume of 340 uL of citrated blood is pipetted to the study cup, recalcified by the addition of 20 uL of 0.2M calcium chloride, and then activated with a kaolin-cephalin reagent. Kaolin is a mineral primarily composed of hydrated

aluminum silicate, a negatively charged molecule that can initiate the intrinsic coagulation pathway by activating Factor XII. Precise proportioning of the blood and kaolin-cephalin reagent is important for accurate and reproducible TEG results.[25]

Rapid TEG (r-TEG) utilizes tissue factor instead of the kaolin-cephalin reagent to activate blood coagulation. The test can be performed faster than conventional TEG.

Rotational thromboelastography, also known as rotational thromboelastometry (RoTEM), utilizes an oscillating pin that rotates +/- 4 degrees 45' every 6 seconds while maintaining the cup in a stable position. In this assay, some different activator reagents are utilized to investigate specific components of the coagulation pathway.

We have lack of data from India and developing countries, where resources are limited and patients have little access to health insurance. Extra product support may increase financial burden in addition to the transfusion associated risks.



TEG® Hemostasis Analyzer Tracing Image and TEG® LY30 Clot Breakdown Diagram reproduced from Haemonetics Corporation. TEG® and Thromboelastograph® are registered trademarks of Haemonetics Corporation in the US, other countries, or both.

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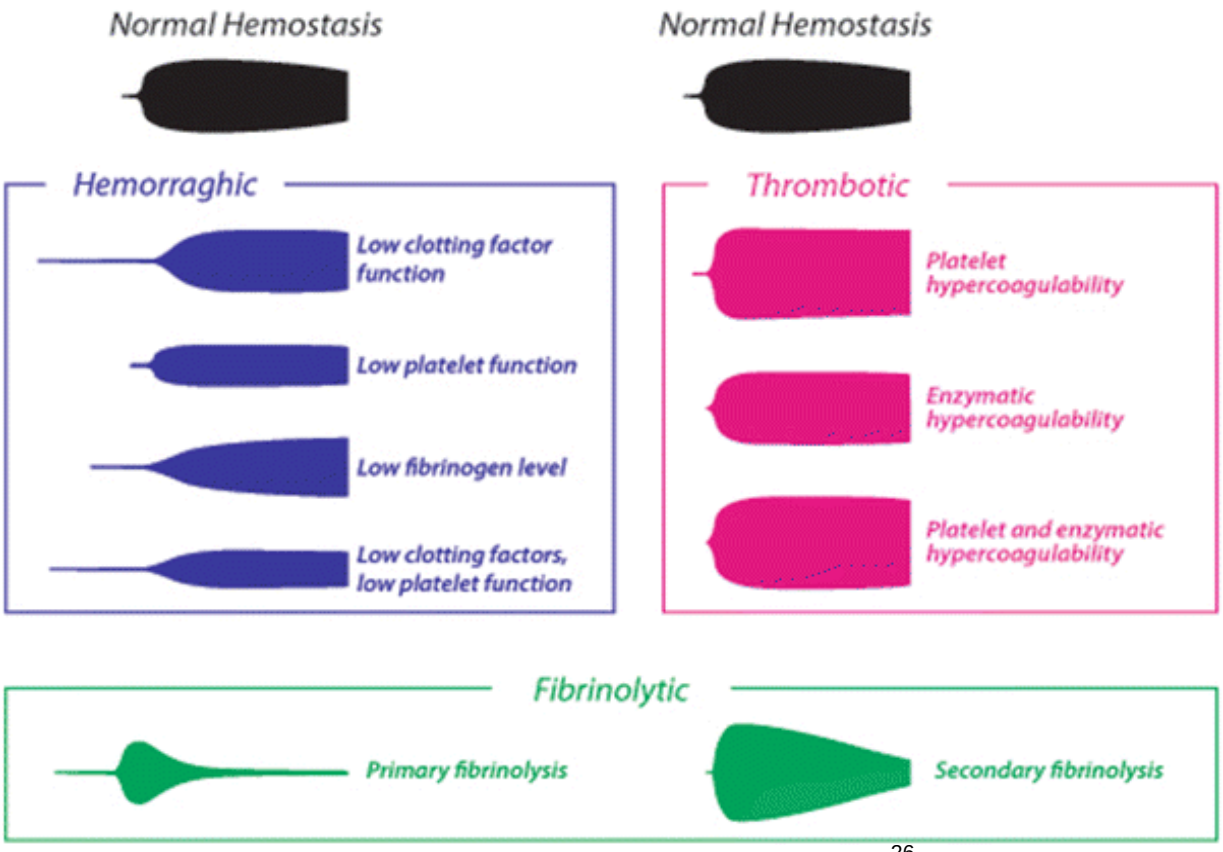

EXAMPLE OF NORMAL AND ABNORMAL TEG TRACINGS[26]

TEG® tracing interpretation images reproduced from Haemonetics Corporation.

TEG PARAMETERS

Components	**Definition**	**Normal Values**	**Problem with**	**Treatment**
R Time	Time to start forming clot	5-10 minutes	Coagulation factors	FFP
K Time	Time until clot reaches a fixed strength	1-3 minutes	Fibrinogen	Cryoprecipitate
Alpha Angle	Speed of fibrin accumulation	53-72 degrees	Fibrinogen	Cryoprecipitate
Maximum Amplitude (MA)	Highest vertical amplitude of the TEG[14, 22]	50-70 mm	Platelets	Platelets
Lysis at 30 minutes (LY30)	Percentage of amplitude reduction 30 minutes after maximum amplitude	0-8%	Excess fibrinolysis	Tranexemic Acid and/or Aminocapric Acid

Modified from References[27,28]

6.3 AIMS AND OBJECTIVES

To assess the role of TEG in patients in defining product requirement for achieving haemostasis in comparison to Conventional Coagulation Test (PTI/INR and platelets) in patient with cirrhosis who are undergoing surgery or radiological interventions.

7. MATERIAL AND METHODS

7.1 SOURCE OF DATA

In patient department and Out patient department record of patients of General Medicine, Gastroenterology ,Cardiology ,Surgery and Intervention Radiology at Dayanand Medical College and Hospital, Ludhiana.

7.2 METHOD OF COLLECTION OF DATA

Cases shall be selected on the basis of criteria set in inclusion and exclusion criteria for the study and TEG shall be performed in selected patients.

INCLUSION CRITERIA

1. Age >18yrs
2. Diagnosis of cirrhosis documented by clinical or imaging (USG/fibroscan) or liver biopsy
3. Undergoing invasive procedure like ascitic tap /pleural tap (paracentensis) ,percutaneous drainage of abscesses, collections, central line insertion ,dialysis catheter insertion ,coronary angiography, PTCA, surgical procedure like biopsy from various sites ,debridement ,ERCP with sphincterotomy, treatment of HCC like alcohol injection, TACE,TARE
4. patients with INR > 1.5 or patients with Platelet <50x10 ^{3}/ul

EXCLUSION CRITERIA

- Patient without clinical/imagining evidence of cirrhosis
- On going bleeding
- Current thrombotic events (arterial/venous clot)
- Antiplatelet or coagulant therapy at time of enrollment
- Hemodialysis in the previous seven days
- Patient with primary bleeding disorder/ bone marrow disorder
- Patient with any blood transfusion during hospitalization before TEG
- Hypercoagulable state like Polycythemia vera
- Chronic renal failure

- Pregnancy
- Sepsis
- DIC
- Shock

NO OF PATIENTS

The study will be conducted on consecutive cirrhotic patients undergoing intervention /surgeries between 15th September 2022 to 31st July 2023

STUDY DESIGN

It is a prospective, observational, cohort study where in all consecutive patients with cirrhosis under going invasive procedure who need blood products in view of coagulopathy as defined by conventional coagulation tests, shall undergo Thrombelastography .TEG parameters shall then be used to guide product transfusion and outcomes like post procedure bleed and TRALI /TACO shall be assessed.

The invasive procedures being performed can be classified on basis of bleeding risk as [21]

1.Low Risk of bleeding (bleeding risk <3%)

- Paracentesis
- Thoracentesis
- Central vein cannulation
- TIPSS

2.High risk of bleeding(>3%)

- Endoscopic varices banding'
- Radiofrequency ablation
- Biopsy
- Drainage of other sites
- ERCP with spincterotomy

INDICATION OF TRANSFUSION

TEG RESULT	**TREATMENT**
R> 15 mins	4 UNITS OF FFP
MA ≤40 mm	1SDP / 4RDP
ANGLE < 45 degrees	0.06 units/kg cryoprecipitate

CCT RESULT	**TREATMENT**
PTI/INR >1.5	FFP at dose 15ml/kg ideal body weight
PLATELETS <50X 10^3/ul	1SDP/ 4RDP

One unit of FFP – 250 ml/unit

One unit of cryoprecipitate- 20-40 ml/unit

One unit of SDP – 200 ml/unit

One unit of RDP – 100 ml/unit

In patient with ascites, for better standardization ,the amount of blood products administered in patients shall be calculated according to ideal body weight of the patient using the Devine formula as follows:-

Male ideal body weight = 50 Kg + 2.3 Kg per inch over 5 feet

Female ideal body weight = 45.5 kg + 2.3 Kg per inch over 5 feet

OUTCOME MEASURES

Primary Outcome Measures

1. Amount of FFP (Fresh Frozen Plasma), platelets and cryoprecipitates transfusion in ml, as guided by TEG, compared to that planned with CCT

Secondary Outcome Measures :

1. Number of patients with bleed post procedure, defined as overt bleeding or haemoglobin drop requiring transfusion with a target of 8 g/dl [Time Frame: 5 days]
2. Incidence of TRALI (Transfusion associated lung injury) and TACO (Transfusion associated circulatory overload) [Time Frame: 6 hours]
3. Transfusion related side effects, defined as any side effect occurring within 6 hours of blood products infusion
4. Procedure related complications other than bleeding

STATISTICAL ANALYSIS

Data will be described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. All statistical calculations will be done using (Statistical Package for the Social Science) SPSS 21version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

SAFETY

At the end of the procedure, patients to be clinically reassessed daily for 5days or until discharge. Any bleeding episode would be recorded, in the case of transfusion, amount of blood and transfusion-related side effects to be noted.

LIMITATIONS

- The test is still an ex vivo simulated haemostatic challenge, that is not without potential biases.
- Results can be altered if the patient is hypothermic as the sample of blood is tested at 37^{o}C, and the sample should be analysed expediently after drawing the blood.
- There is a possibility for human error depending on the level of experience of the technician performing the evaluation.
- Information on the initial clot formation can be obtained quickly on a TEG study, but to get the full information from a TEG the sample must be evaluated for 60 minutes to get the CL30 and CL60 values which indicate the percentage of lysis of the clot after reaching its maximum amplitude at 30 and 60 minutes.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

No

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Yes, Attached herewith

APPENDIX

INVESTIGATION	**COST**
1) TEG	Rs. 5100 (kaolin based)
2) PTI/INR	Rs.230
3) PLATELETS	Rs.100
BLOOD PRODUCTS	
Fresh frozen plasma	Rs. 1200 per unit
Cryoprecipitate	Rs.1300 per unit
SDP	Rs. 12700 per unit
RDP	Rs. 1540 per units

8. LIST OF REFERENCES

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PERFORMA

S.No.

NAME

AGE

GENDER

MRD NO

ADDRESS

CONTACT NUMBER

BODY WEIGHT

IDEAL BODY WEIGHT – CIRRHOTIC WITH ASCITES

ETIOLOGY

- HEPATITIS B
- HEPATITIS C
- ALCHOLIC LIVER DISEASE
- NON-ALCHOLIC STEATO HEPATITIS
- INBORN ERRORS OF METABOLISM
- AUTOIMMUNE LIVER DISEASE
- WILSONS DS

ASCITES

HEPATIC ENCEPHALOPATHY

MELD SCORE

CHILD-PUGH SCORE

CHILD-PUGH CLASS

Signature of Candidate Signature of Supervisor

PATIENT WITH HCC YES/NO

HEMOGLOBIN (gm/dl)

WBC (10^3/ul)

PLATELET COUNT (10^3/ul)

PTI/INR

TEG PARAMETERS – R VALUE (MINS)

ALPHA ANGLE (DEGREE)

MAX AMPLITUDE (MM)

	Blood products requirement as per CCT	Blood products requirement as per TEG
Total amount of FFP infused, mL		
Total amount of PLTs infused, Units		
Total cost of transfusion		
Net Cost		
Bleeding event		
Transfusion related side-effect		

Signature of Candidate

Signature of Supervisor

INFORMED PATIENT CONSENT

Date: _____

I…….D/o, W/o, S/o……..…… am willing to participate in the study **"TO STUDY THE ROLE OF THROMBOELASTOGRAPHY (TEG) IN CORRECTION OF COAGULOPATHY IN PATIENTS OF CIRRHOSIS UNDERGOING INVASIVE PROCEDURES"** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

……. ……

Signature of the Witness Signature of the patient

Name:

Signature of Candidate **Signature of Supervisor**

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____
निवासी _____
इस शोधकार्य "**TO STUDY THE ROLE OF THROMBOELASTOGRAPHY (TEG) IN CORRECTION OF COAGULOPATHY IN PATIENTS OF CIRRHOSIS UNDERGOING INVASIVE PROCEDURES"** में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____ _____
गवाह के हस्ताक्षर रोगी के हस्ताक्षर/अंगूठे का निशान
नाम: नाम:

_____
अन्वेषक के हस्ताक्षर

_____
विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____

“TO STUDY THE ROLE OF THROMBOELASTOGRAPHY (TEG) IN CORRECTION OF COAGULOPATHY IN PATIENTS OF CIRRHOSIS UNDERGOING INVASIVE PROCEDURES” ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____ _____

ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਪਤਾ _____ ਪਤਾ _____

_____

ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____

ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ